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Plantar Pressure, Cutaneous Sensation and Stochastic Resonance: An Examination of Factors Influencing the Control and Perception of Posture

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PLANTAR PRESSURE, CUTANEOUS SENSATION AND STOCHASTIC RESONANCE:

AN EXAMINATION OF FACTORS INFLUENCING THE CONTROL AND PERCEPTION OF POSTURE

A Dissertation Presented

by

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ABSTRACT

PLANTAR PRESSURE, CUTANEOUS SENSATION AND STOCHASTIC RESONANCE:

AN EXAMINATION OF FACTORS INFLUENCING THE CONTROL AND PERCEPTION OF POSTURE

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The goal of this dissertation was to understand how people control posture in the context of sensory loss. To do so we explored three potential influences on the detection of external information and how they relate to the control of posture and perception of body orientation: 1) does changing posture alter the forces under the foot, and do these changes impact the ability to detect external vibrations? 2) Does decreasing the temperature of the foot influence the ability to detect external vibrations, the perception of body orientation, and the control of posture? And 3) does stochastic resonance (SR) improve the perception of body orientation and the control of posture when the sensory thresholds are elevated to clinical levels through cooling of the feet?

The results of the experiments indicate that: 1) increasing the pressure under the feet, elicited by changes in posture, elevates the cutaneous sensory threshold, and that the forefoot appears to be more sensitive than the rearfoot to changes in weighting; 2) decreasing the temperature of the skin elevates cutaneous sensory thresholds, and impacts postural control by constraining the fluctuations of the medial-lateral center of pressure;

and 3) applying SR to the soles of the feet improves the ability to perceive body position, with greater amounts of skin cooling resulting in greater improvements in postural performance due to SR.

This dissertation demonstrates that decreasing plantar loading lowers cutaneous sensory thresholds, indicating that the changes in postural fluctuations frequently observed among those with clinical sensory loss may serve as a mechanism that allows for improved access to external information if they prove to reduce the pressure under sensory impaired portions of the feet. Additionally, we add to the growing body of literature identifying SR as a means to improve postural performance when cutaneous sensory function is impaired. From a clinical perspective, the results presented here indicate that aids designed to apply SR to the soles of the feet, as a means to improve posture and gait, should modulate their signal such that they apply a signal amplitude appropriate to the amount of loading the foot experiences.

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CHAPTER I

DEVELOPMENT OF THE PROBLEM

1.1 Background

The control of upright standing posture is a fundamental task humans perform to accomplish a variety of activities of daily living. The United States Centers for Disease Control and Prevention estimate there are 30 million Americans who suffer from cutaneous sensory loss in their feet (Dillon, Gu, Hoffman, & Ko, 2010), a condition which is associated with dramatic reductions in an individual's ability to control upright posture. Cattaneo and Jonsdottir (2009) reported that among those with cutaneous sensory loss, impairment to balance control and mobility ranked as major factors for reducing quality of life. Therefore, studies that seek to understand of how sensory loss directly impairs the control of posture may lead to improved methods for enhancing the lives of individuals with cutaneous sensory loss. Additionally, this information can provide a basis for evaluating biomedical techniques aimed at improving postural control through amelioration of the underlying physiological dysfunction. This could have a significant impact in lowering the $19 billion annual cost associated with fall-related injury (Stevens, Corso, Finkelstein, & Miller, 2006), costs that are predicted to escalate to over $50 billion by 2050 (Stevens et al., 2006).

Developing a better understanding of how cutaneous sensation of the feet impacts the control of posture has the potential to improve quality of life and mitigate health care costs associated with balance loss. This improved understanding can, in turn, lead to the development of biomedical aids, such as shoes that deliver signals that directly address

the critical sensory deficits. Although research has shown that many clinical conditions (e.g., multiple sclerosis and stroke) exhibit concurrent reductions in cutaneous sensation and postural stability, this connection is poorly understood. There is limited evidence that during standing, body position influences postural center of pressure (COP) dynamics (Riccio, 1993); these changes in COP dynamics may serve a functional role in enhancing the ability to identify external stimuli, in their environment. However, there do not appear to be any published studies that have examined how COP dynamics impact the ability to identify external stimuli.

To this end, the studies outlined in this dissertation will contribute novel insights into how cutaneous sensory ability and postural configuration influence the control of the postural COP and perception of body orientation. This set of studies will focus on three key areas: 1) the effect of changing the pressure distribution under the foot on the ability to detect somatosensory stimuli; 2) the effect that a controlled cooling of the feet has on the ability to detect somatosensory stimuli; and 3) the ability of stochastic resonance (SR), a technique reported to improve stimulus detection (Collins et al., 2003), to improve the control of the postural COP and the perception of body orientation. These studies will provide new information as to how postural pressure and sensory function interact in the identification of external stimuli, and what role they play in the control and perception of upright posture.

1.2 Cutaneous Sensation

The successful control of upright standing is influenced by several sensory inputs, including vision, vestibular function and cutaneous sensation. The manner in which the

cutaneous sensory receptors of the foot identify stimuli has, so far, only been assessed in unweighted (supine) conditions (Kennedy & Inglis, 2002). During walking, however, Nurse and Nigg (2001) reported an increase in pressure under sensory impaired portions of the foot compared with the pressure under the same portion of the foot when sensation is not impaired. This research suggests, as Inglis and colleagues have argued (Inglis, Kennedy, Wells, & Chua, 2002; Kennedy & Inglis, 2002), that sensory function assessed in the supine position may not be representative of sensory function in standing postures. Therefore, changes in cutaneous sensation in the supine position likely fail to reflect how impaired sensory ability affects postural control (Inglis et al., 2002; Patel, Magnusson, Kristinsdottir, & Fransson, 2009), a process carried out while the foot is weighted.

Further support that plantar pressure influences the detection of external stimuli comes from two studies that examined the ability of stochastic resonance (SR), a biomedical technique that applies subsensory white noise signals to the skin and has been shown to improve temporal (Galica et al., 2009) and spatial (Stephen et al., 2012) gait patterns in elderly populations. These studies found that different SR magnitudes were needed during different portions of the gait cycle (swing, single-support and dual-support); that is, one magnitude was not suitable for the entire gait cycle, suggesting that the magnitude of the minimum detectable stimulus changes along with plantar pressure. This is further supported by pilot work for this dissertation (1.1), which demonstrated increased magnitude of the minimum detectable sensory stimulus when posture changed from supine to quiet standing, indicating that postural configuration and the associated changes in pressure underneath the foot impact stimulus detection. The first study in this dissertation aims to further explore how the ability to detect external stimuli with the foot

responds to changes in plantar surface pressure during upright standing tasks; in doing so, we will address a critical gap in the literature.

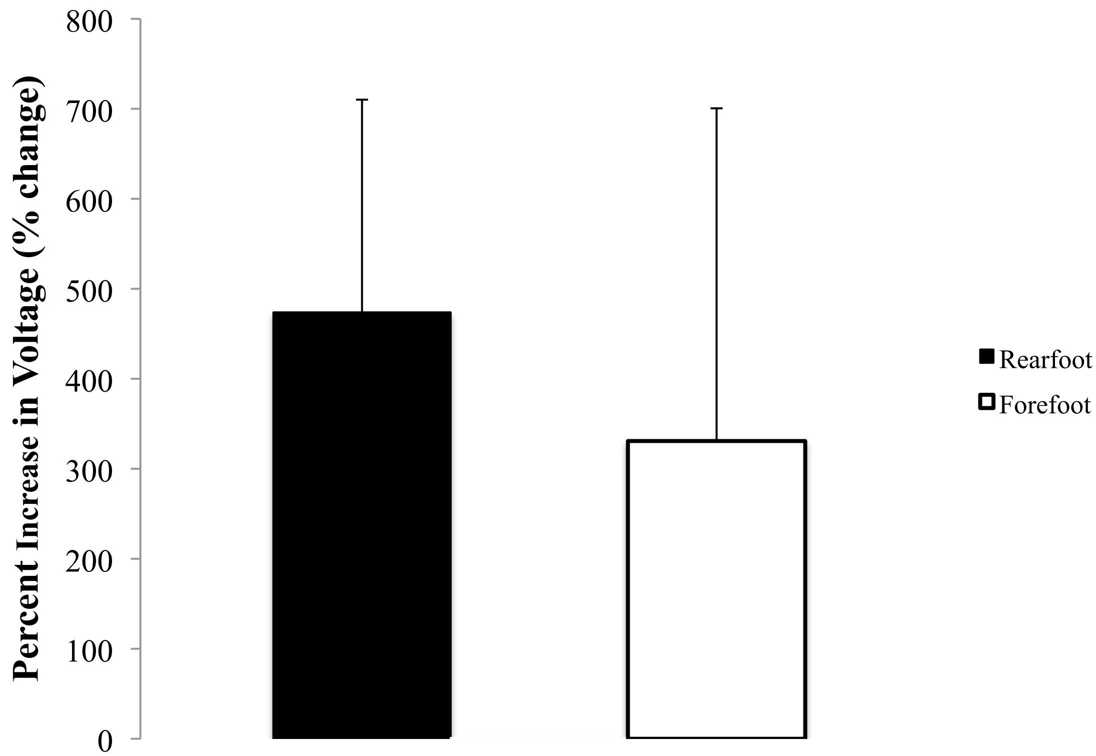

Figure 1.1: Percent Increase in Minimum Detectable Stimulus Fore- and Rearfoot: Increases in the voltage of the minimum detectable stimulus. Positive values indicate stronger stimulus voltage in standing compared to supine. Mean (SD). Data based on pilot study of n=3 healthy controls.

Beyond expanding the understanding of how functional postures change the ability to detect external stimuli, it is also important to understand how changes in sensory function impact the control of posture and body orientation. Expanding this understanding is critical, as there are increasing number of individuals with primary medical conditions for which cutaneous sensory impairment is a debilitating comorbidity, such as multiple sclerosis (Citaker et al., 2011; Van Emmerik, Remelius, Johnson,

Chung, & Kent-Braun, 2010) and diabetes (Bonnet, Carello, & Turvey, 2009). Gaining a better understanding of how cutaneous sensory loss influences the control of posture, and how these losses might be alleviated, has the potential to improve the quality of life for individuals with sensory impairment. The impact of cutaneous sensory function on postural control has been discussed in the literature; though this has primarily been done in the context of clinical disorders whose symptoms include simultaneous deficits in sensory function and postural control (Thoumie & Mevellec, 2002; Van Emmerik et al., 2010). This clinical work allows for an understanding of how the loss of cutaneous sensation impacts postural control; it does not however allow for an understanding of how cutaneous sensory impairment directly influences the control of posture. The reason for this is many clinical disorders exhibit multiple comorbidities that also affect postural control. A more complete understanding of how cutaneous sensory function impacts the control of the postural COP and perception of body orientation would provide valuable information as to how potential improvements in external stimuli detection, through SR, can potentially improve the quality of life of individuals with cutaneous sensory loss.

Inducing reduced cutaneous sensory function in otherwise healthy populations is an advantageous approach, as actively reducing cutaneous sensation allows for the assessment of the causal relationship between sensory function and postural control. Systematically decreasing skin temperature has been reported to impair the ability to detect external cutaneous stimuli (Figure 1.2) (Weitz, 1941, 1942). The results from studies using this technique show that decreasing skin temperature from a “normal” operating range can have dramatic effects on the ability to identify external vibrating stimuli. A 12-degree Celsius reduction in skin temperature has been reported to raise the

magnitude of the minimum detectable stimulus by up to 400% (Weitz, 1941). Furthermore, it has been reported that lowering the skin temperature has a greater impact on reducing stimulus detection in women than in men (Liou et al., 1999). In addition to effects on stimulus identification it has been reported that lowering skin temperature impairs the perception of postural orientation (Fujiwara et al., 2003). Fujiwara et al. (2003) reported that cooling the feet to 1 degree Celsius resulted in significant impairment in the ability to reposition the COP in relation to a reference position. The use of stepwise, controlled cooling of the feet will thus serve as a platform to reduce participants' ability to detect cutaneous stimuli with the feet, inducing temporary sensory loss in otherwise healthy individuals.

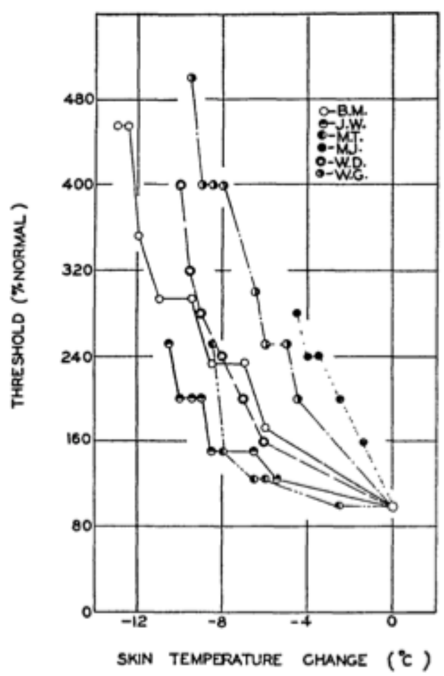

Figure 1.2: Change in Skin Temperature v. Sensory Threshold (%) (Weitz, 1941)

1.3 Postural Control

The control of upright standing posture is an essential component of many activities of daily living (Maki, Holliday, & Topper, 1994), as humans utilize a variety of upright postures everyday (e.g., quiet upright standing, leaning and reaching), with some being more challenging than others. These different postural configurations have been reported to alter the temporal patterns of the postural COP (Riccio, 1993). Developing an understanding of how postural fluctuations impact the identification of external stimuli will generate important information about the functional role of plantar pressure dynamics in the control of posture. For example, exploring how the pressure patterns under the feet influence the ability to detect cutaneous information may provide evidence that postural control dynamics are continually tuned in a way to reliably access sensory stimuli. Evaluating the link between postural configuration and the detection of stimuli may also provide evidence that posture is controlled in a manner that affords the identification of external stimuli, suggesting a mutuality between perception and action: we act in order to perceive and perceive in order to act (Gibson, 1979).

The assessment of postural control can be done through a number of mathematical techniques. However, the specific questions being explored in this dissertation relate to how the COP dynamics are altered when sensory ability is diminished. In order to best evaluate these questions, multiscale entropy (MSE) of the COP time series will be assessed. MSE is a measure that evaluates point-to-point fluctuations in a time series and allows for the quantification of how the COP dynamics change over a variety of time scales (Costa, Goldberger, & Peng, 2002, 2005; Costa et al., 2007; Gruber et al., 2011; Manor et al., 2010). The evaluation of many time scales is important here because control

of the COP does not operate at fixed frequencies, nor do the receptors which identify stimuli (Bolanowski, Gescheider, Verrillo, & Checkosky, 1988; Riccio, 1993). MSE has also been reported to be more sensitive than other COP measures in differentiating between clinical sub-groups (Gruber et al., 2011). This additional sensitivity means that MSE can transition well between studies that seek to provide fundamental information about processes and studies that seek to understand how system complexity relates to quality of life improvements in clinical applications.

1.4 Stochastic Resonance

Stochastic resonance is a physical phenomenon by which non-linear signal transmission is enhanced through the presence of low-level white noise (Benzi, Sutera, & Vulpiani, 1981; Collins, Chow, & Imhoff, 1995b; Nicolis, 1982). This enhancement is thought to occur by bringing the original signal to the activation threshold value, such that events that previously produced a sub-threshold signal now reach threshold. An example of the manner in which SR is thought to function can be seen in Figure 1.3.

When elicited through mechanical stimulation, SR has demonstrated improvement in postural control in a variety of populations, including young, healthy participants (Priplata et al., 2002), elderly participants with and without a history of falls (Costa et al., 2007; Priplata, Niemi, Harry, Lipsitz, & Collins, 2003), and those with diabetes and stroke (Priplata et al., 2006). Collins et al. (2003) concluded that the observed improvements in postural control are brought about through improvements in tactile sensation. While SR has been shown to improve postural control in clinical populations, it remains unknown whether SR will improve the control of the postural

COP and perception of body orientation when the ability to identify external sensory stimuli is systematically diminished in otherwise healthy individuals.

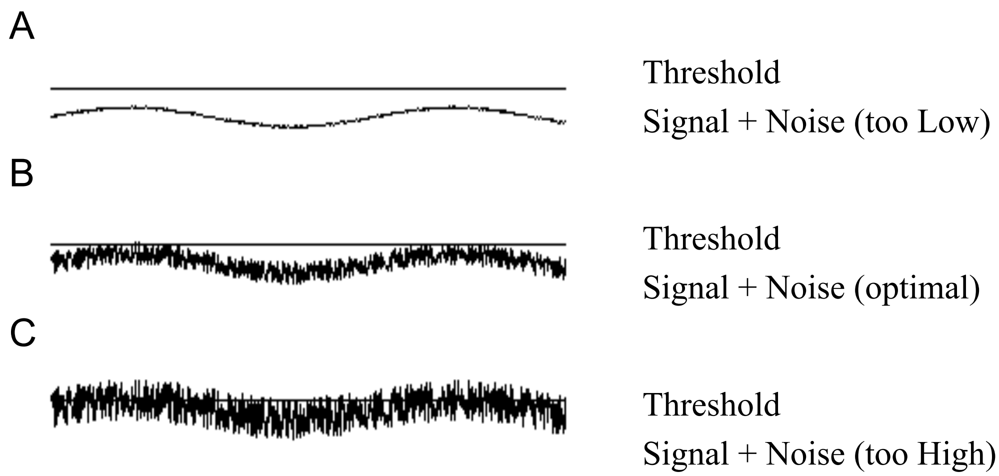

Figure 1.3: Description of Optimal Noise Level. A) Low level of noise added to the normal signal is too low to reach threshold. B) Noise level is optimal, such that it causes the signal to reach threshold at its peaks. C) Noise level is too high, such that normal fluctuations in the signal, which should remain sub-threshold, are not (adapted from: Van Emmerik, Jones, Busa and Baird, 2013).

1.5 The Relationship Between Cutaneous Sensation and Postural Control

The link between action and perception has been extensively explored in the study of haptic perception, whereby individuals are able to identify basic properties of objects through touch (Turvey, 1996). Groups with diminished sensory function have revealed altered COP function (Van Emmerik, Jones, Busa, & Baird, 2013; Van Emmerik et al., 2010), though there exists the possibility that the COP dynamics are altered in a functional manner, such as to enhance the detection of environmental stimuli. Altered COP dynamics may result from changes in the perception of body orientation, and this has been shown in those with artificially induced sensory impairment (Fujiwara et al.,

2003). The notion that we can modulate our COP patterns in a meaningful way is supported through research demonstrating that the postural COP can be modulated in a way to identify information about external objects (Palatinus, Dixon, & Kelty-Stephen, 2012); however, the manner in which impaired ability to detect cutaneous sensory stimuli impacts COP fluctuations remains unclear.

The role of cutaneous sensory function in the control of posture appears to be mediated, at least in part, by haptic perception; therefore, it is important to gain further insight into how sensory status impacts both perception and dynamics of postural control. At present, Fujiwara et al. (2003) have performed the only work examining how impairing foot sensory function (through cooling) impacts the ability to recreate postural configurations. This study reported that cooling the foot by a significant amount elicits greater errors in a postural repositioning task than when the foot temperature was not cooled.

Improved understanding of the relationship between the ability to detect external stimuli through the plantar surface of the foot and the intrinsic control of posture would provide evidence as to how information gathered from the feet is used to control posture. Enhancing the ability to detect cutaneous stimuli may allow for significant improvement in the control of posture. However, it would be remiss to think that only somatosensory information influences the control of posture, as cues from additional systems, e.g., vision and vestibular function, are integrated with somatosensory information in the control of upright standing (Horak & Macpherson, 2010).

1.6 Integration of Multisensory Information and the Control of Posture

As previously noted, the control of posture is influenced by sensory information from several sources: cutaneous receptors in the skin, muscle spindles, vision, and the vestibular system. It is through the integration of all these types of information that we are able to gain knowledge of how our body interacts with the environment (Stoffregen & Riccio, 1988). Evidence that vision is used in the control of posture can be seen in two types of studies: 1) those which measure the postural response to different visual information (Duarte & Zatsiorsky, 2002; Wade & Jones, 1997), and 2) those which quantify how the ability to perceive body orientation changes when vision is removed (Fujiwara et al., 2003). For the purpose of this dissertation we will only discuss the latter, as it relates to the problem of creating tasks designed to provide insight into the function of cutaneous sensation in the control of posture.

In particular, we are interested in designing tasks that place maximal reliance on the role of cutaneous sensory feedback. This isolation is complicated, however, for when a specific sensory system is impaired, the body offsets the loss through increased reliance on other sources of sensory information. For example, when a person has lost the ability to identify information through touch they become more reliant on visual information (Backman & Dixon, 1992). These compensatory actions are triggered when a particular sensory modality becomes less reliable (Jeka, Oie, & Kiemel, 2000; Kiemel, Oie, & Jeka, 2002; Polastri, Barela, Kiemel, & Jeka, 2012). This appears to occur through a reweighting process, as opposed to a total elimination, whereby the information obtained from a particular sense is valued differently than it normally would be (Backman & Dixon, 1992). Intra- and intermodal weighting of sensory information appears to be

modulated in a way such that preference is given to more reliable sensory processes (Jeka et al., 2000; Polastri et al., 2012).

Fujiwara et al. (2003) found that participants were able to accurately recreate postural configurations when the ability to detect somatosensory stimuli was impaired through cooling of the feet but vision was allowed. However, when participants had vision occluded in addition to the cooling of the feet they were not able to accurately reposition themselves, suggesting that in otherwise healthy individuals intact vision can compensate for somatosensory loss. Additionally, it has been reported that greater errors are observed when participants are instructed to recreate postures that place the COP in a location close to that which occurs during quiet standing, compared to repositioning tasks where the COP was to be placed further from the quiet standing position. These findings suggest that when vision is occluded, other sensory structures are able to provide supplemental sensory information to cutaneous sensation, allowing for more accurate positions sense.

1.7 Approach

Collectively, the three studies that comprise this dissertation aim to explore the ways in which sensory ability and pressure patterns under the foot influence the perception and control of posture. Each study will use young healthy women to explore how the intrinsic dynamics of controlling posture change as the ability to identify cutaneous stimuli is artificially impaired. This will, in turn, provide a framework to explore methods that strive to improve control and perception of the postural COP in cases where an individual's ability to detect external stimuli is impaired due to clinical

disorder. There are three distinct goals for the proposed studies, and they will be examined in step-wise fashion, each building on the previous: 1) determine how pressure patterns under the feet influence the detection of cutaneous stimuli, 2) determine what effect impairing cutaneous sensation, through reduction in the skin temperature of the plantar surface of the foot, has on the control and perception of posture, and 3) determine the ability of stochastic resonance to improve control and perception of posture, specifically in the presence of controlled reductions of temperature-mediated sensory loss.

1.8 Statement of the Problem

Currently, there is a lack of understanding of how a reduction in sensory ability impacts the perception and control of posture. There are many studies that have observed coincidental reductions in the control of posture and the ability to detect plantar surface stimuli (Benedetti et al., 1999; Bonnet et al., 2009; Citaker et al., 2011; Hohne, Ali, Stark, & Bruggemann, 2012; Van Emmerik et al., 2010). However, these studies all examined clinical populations (e.g., individuals with multiple sclerosis or diabetes), which often have comorbidities other than cutaneous sensory loss that may also result in diminished control of posture. Currently, we remain unable to establish with any certainty what specific role impaired plantar sensation has on the control of posture. By examining how changes in the ability to access environmental information with the plantar surface of the feet impacts healthy individuals' control of posture, the proposed studies will provide the basic research that is needed to improve our understanding of the relationship between cutaneous sensory function and postural control.

1.8.1 Study One: The Effect of Load on Plantar Surface Cutaneous Sensation

The aim of this study is to provide insight into how changing the pressure under the feet impacts the ability to detect external sensory stimulation. This will be achieved through assessing three postural configurations that change the pressure distribution under the feet: supine, quiet standing, and forward lean. The manipulation from non-standing to standing postures fundamentally changes the vertical force underneath the feet; comparison of these conditions will therefore allow us to determine whether there are fundamental changes in the ability to detect cutaneous stimuli when the foot is in a weight-bearing posture. The forward lean condition has been suggested to change the frequency of the COP dynamics to that of higher frequency content (Riccio, 1993). Using this postural configuration enables us to test if changing the plantar pressure distribution impacts the ability to detect cutaneous stimuli.

A vibrating tactor (Engineering Acoustics Inc., Casselbury, FL) will be used to present vibrating stimuli to the feet. White noise vibrations in the range of 30-350 Hz will be applied to both the forefoot (3rd metatarsal) and rearfoot (calcaneous), and participants will be instructed to identify the presence of these signals. This particular frequency band was chosen as it should elicit a response from all the known cutaneous sensory organs of the foot, such as Meissner's and Pacinian corpuscles (Bolanowski et al., 1988; Wells, Ward, Chua, & Inglis, 2003). The minimum detectable stimuli identified with the tactors will be compared to measurements made with a biothesiometer (Bio-Medical Instrument Co. Newbury, OH), a commonly used clinical device used to assess cutaneous sensory function. Additionally, the results of this study will provide context for the interpretation of the data in the subsequent studies, as understanding how changes in pressure

distribution under the feet impacts detection of external stimuli will, in turn, provide insight to how changes in the ability to detect external stimuli may influence postural dynamics.

1.8.1.1 Rationale

Changes in postural configuration are thought to alter the temporal structure of how the COP is modulated in upright standing (Riccio, 1993). That is, leans toward the anterior and posterior boundary increase the high-frequency components of the COP fluctuations. Additionally, studies of persons with clinical conditions have reported reductions in postural control and diminished ability to detect cutaneous stimuli (Citaker et al., 2011; Van Emmerik et al., 2010). The existing work does not, however, address how pressure changes under the feet influence the ability to detect external stimuli. This study will contribute to the understanding of how changes in the pressure distribution under the foot influence the ability to identify external stimuli.

1.8.1.2 Research Question

How does changing the pressure distribution under the foot, through the manipulation of posture, affect the ability to identify somatosensory stimuli with the plantar surface of the foot?

1.8.1.3 Hypotheses

The general hypothesis for this study is that when pressure is increased on any portion of the foot, a greater minimum stimulus will be required for detection in that

same region. This hypothesis is supported by work that examined the use of SR in gait, where the magnitude of stimulation to the feet was varied during three portions of the gait cycle: single-support, dual-support, and swing (Galica et al., 2009; Stephen et al., 2012). The researchers found that this variation was necessary in order to keep the stimulation level at 90% of the minimum detectable stimulus. These findings were further supported by pilot work for this dissertation, which observed increases in the minimum detectable stimulus in postures that resulted in greater pressure under both the fore- and rearfoot (Figure 1.1). To test this general hypothesis, we will examine how changes in plantar pressure impact the minimum detectable stimulus. Additionally, a series of individual comparisons will be made to parse out how changing the pressure on different portions of the foot impacts the ability to detect environmental stimuli. These comparisons will test the following sub-hypotheses:

a) The three postures: supine, quiet standing, and forward lean will exhibit differences in the minimum detectable stimulus in both the fore- and rearfoot locations.

b) The magnitude of the minimum detectable stimulus will exhibit a positive relationship with the plantar pressure under the foot. That is, the more pressure under the foot the greater the minimum detectable stimulus will be.

c) Quiet standing will require the greatest magnitude for the minimum detectable stimulus in the rearfoot, compared to the supine and forward lean postures. In quiet standing, the magnitude of the minimum stimulus required in the forefoot will be greater than in the supine position but less than the forward lean.

d) The supine condition will have the lowest threshold for stimulus detection, in both the fore- and rearfoot locations.

e) The forward lean will require a greater stimulus magnitude for detection in the forefoot compared to both supine and quiet standing postures. In forward lean, the rearfoot stimulus magnitude will be increased over the supine position, but lower than the quiet standing posture.

f) The biothesiometer and the C-2 tactors will have a significant, strong positive correlation, indicating that the C-2 tactors are a reliable tool for assessing the minimum detectable stimulus.

1.8.2 Study 2: The Effect of Impaired Sensory Function on the Control and Perception of Upright Posture

The aim of this study is to assess the effects of reduced cutaneous function on the control and perception of postural COP. Following from the work of Weitz (1941), the ability to detect sensory stimuli will be decreased by cooling the skin in a controlled manner. We will then assess the influence of these temperature-mediated sensory changes on the control of the postural COP and perception of body orientation. This experiment will consist of three parts. The first portion of the experiment is psychophysical in nature and will determine whether cooling the feet changes the magnitude of mechanical stimuli that need to be applied to the foot for identification. The second part of the study will examine how the ability to reposition the body is influenced by systematically cooling the feet to different temperatures. The final portion of this study will examine how the complexity of the COP time series changes with decreased sensory ability.

1.8.2.1 Rationale

Gaining an understanding of the relationship between sensory ability and postural control will allow for insight as to how sensation, perception and control are linked in standing tasks. Using a paradigm that allows for graded changes in sensory function will provide a fundamental understanding of how detection of cutaneous information with the feet impacts the control of posture.

1.8.2.2 Research Questions

How does decreased skin temperature through cooling the feet affect: 1) stimulus detection threshold, and 2) the control of posture and perception of body orientation. These questions will be addressed in 3 stages:

1) The magnitude of the minimum stimuli will be identified during supine and quiet upright standing postures. The sites of stimulation will be the same as Study 1, bilateral in the fore- and rearfoot. The stimulation frequency band will be 30-350 Hz, allowing for activation of all known sensory organs. This will be repeated at the naturally occurring skin temperature (ST-0) of the feet as well as 4 (ST-4), 8 (ST-8) and 12 (ST-12) degrees Celsius below ST-0, as these temperatures have been previously reported to increase the magnitude of the minimum detectible stimulus. Additionally, biothesiometer measurements will be used to compare how the temperature-mediated changes in minimum detectable stimulus relate to sensory changes in clinical populations.

2) A postural repositioning task will be completed, with vision occluded, to examine how cooling of the feet affects the ability to perceive body orientation. The error

in the repositioning of the COP will provide information as to how changes in skin temperature impact the perception of body orientation.

3) The effect of changing skin temperature on the control of posture will be examined by identifying how each temperature change impacts the complexity of the COP time series.

1.8.2.3 Hypotheses

a) The minimum detectable stimulus threshold will increase as skin temperature decreases. This follows from the work of Weitz (1941, 1942), who demonstrated that, with systematic decreases in skin temperature, consistent increases in the stimulus were necessary before participants could identify the stimulus. Additionally, an exploratory hypothesis will examine the nature of the relationship where it is predicted that the threshold will increase in a curvilinear fashion with temperature.

b) The accuracy of participants' ability to reproduce a prescribed posture will decrease with corresponding decreases in foot temperature. That is, greater errors will be observed in the repositioning of the COP with each successive decrease in temperature-mediated sensory function. Additionally, an exploratory hypothesis will examine the nature of the relationship where it is predicted that the magnitude of the repositioning error will increase with the magnitude of the minimum detectable threshold.

c) The complexity of the COP time series, as assessed by MSE, will decrease with lower temperatures of the foot. This is consistent with previous research, which reports decreases in MSE among individuals with stroke and adolescent idiopathic scoliosis compared to healthy populations (Costa et al., 2007; Gruber et al., 2011). Additionally,

an exploratory hypothesis will examine the nature of the relationship where it is predicted that the complexity of the postural COP will decrease with increases in the minimum detectable stimulus threshold.

1.8.3 Study 3: The Effect of Stochastic Resonance to Restore Postural Control in the Presence of Cutaneous Sensory Loss

The aim of this study is to assess how stochastic resonance can restore postural control when sensory ability is reduced. We plan to address this by applying SR signals to the plantar surface of the feet while the ability to detect cutaneous stimuli has been reduced through a step-wise cooling of the feet. This study builds on Study 2 and assumes that cooling the skin of the feet confers a loss of sensory function and that this impairs postural control. The results of this study will provide information regarding the degree to which SR is able to improve the control of the postural COP and perception of body orientation when the ability to detect cutaneous stimuli with the feet is reduced. The systematic manipulation of sensory ability will broaden our understanding of how SR may be able to improve postural control when cutaneous sensation is degraded.

1.8.3.1 Rationale

The rationale behind conducting this study is that it will allow for a greater understanding of whether, and to what degree, SR has the ability to improve the control of the postural COP and perception of body orientation when the ability to identify cutaneous sensory stimuli is degraded. The temperatures to be used in this study will be selected based on the results of study 2 and will represent clinically relevant sensory loss, assessed through biothesiometer measurement.

1.8.3.2 Research Question

Does stochastic resonance improve the control of the postural COP and perception of body orientation when sensory function and postural control are impaired through a decrease in skin temperature?

1.8.3.3 Hypotheses

a) Trials in which SR signals are applied to the soles of the feet will improve the perception of body orientation compared to when SR is not induced. That is, the application of SR will decrease the error in repositioning the postural COP relative to the reference position compared to the trials when SR is not induced.

b) When sensation has been significantly reduced through cooling of the feet, the application of SR to the plantar surface of the feet will result in improved control of the COP time series during quiet standing. That is, when SR is induced at the foot surface, the complexity of the COP time series will increase, compared with cases when SR is absent.

c) In the presence of stochastic resonance, complexity of the COP time series will increase in a baseline-dependent manner. That is, the more the feet are cooled, and sensory ability degraded, the greater the improvement that will be seen in postural control when SR is applied. This hypothesis is formed on the basis of results presented in Figure 1.2, where a linear decrease in skin temperature appears to confer a nonlinear decrease in sensory function (Weitz, 1941).

1.9 Significance

The set of experiments that make up this dissertation will expand our knowledge as to how variation in the ability to access sensory information through the plantar surface of the feet influences the control of posture. The overarching goal of these studies is to generate new insight in three key areas: 1) the impact that pressure under the feet has on the ability to detect external stimuli, 2) how impairing the ability to detect external stimuli impacts the control of the postural COP and perception of body orientation, and 3) the extent to which stochastic resonance can be used to improve posture when sensory function is impaired. This will be accomplished through the manipulation of postural tasks and altering the sensory ability of the foot through controlled reductions in skin temperature. The experiments outlined above will therefore serve as a means to determine how postural control changes when sensory function is impaired in otherwise healthy individuals. Additionally, this dissertation will examine how stochastic resonance changes the control and perception of posture in the presence of cold-induced sensory loss. By exploring all three of these aspects (posture, sensory function, and stochastic resonance), we will be better able to understand the role of cutaneous sensation in the control of upright standing. The empirical data generated by this series of studies also has the potential to inform important clinical applications, particularly as it may contribute to the design of novel techniques that can be used to improve quality of life for the 30 million Americans who suffer from sensory loss (Dillon et al., 2010).

CHAPTER II

REVIEW OF THE LITERATURE

2.1 Epidemiology of Sensory Loss

The effect of somatosensory loss on the control of posture has been studied in clinical populations; however, it remains unknown if the nature of this relationship is causal. It has been consistently reported that many clinical populations exhibit concurrent impairments in the ability to detect external stimuli as well as postural control including, the elderly (Illing, Choy, Nitz, & Nolan, 2010; Priplata et al., 2003; Sihvonen, Sipila, & Era, 2004), individuals with diabetes (Bonnet et al., 2009; Priplata et al., 2006), persons with multiple sclerosis (Chung, Remelius, Van Emmerik, & Kent-Braun, 2008; Fjeldstad, Pardo, Frederiksen, Bemben, & Bemben, 2009; Martin et al., 2006; Van Emmerik et al., 2010), and those having had a stroke (Geurts, de Haart, van Nes, & Duysens, 2005; Rougier & Boudrahem, 2010). According to the United States Centers for Disease Control and Prevention, cutaneous sensory loss, a predictor of falls, is a comorbidity that impacts 30 million Americans and is a predictor of falls (Dillon et al., 2010). Currently the United States of America spends $19 billion annually on health care costs associated with injurious falls (Stevens et al., 2006). With these costs expected to escalate to over $50 billion by 2050, it is evident that there is an ever-increasing need for approaches that can limit both the risk and associated costs of injury among individuals with cutaneous sensory loss.

2.2 Cutaneous Sensation

The impact of cutaneous sensation of the foot on the control of gait and posture has been studied extensively, but before delving deeper into this literature it is important to gain an understanding of the cutaneous sensory structures of the foot and the types of information that they can access. To this end, we first present a basic discussion of the receptor types in the foot and their distribution. This background will allow for a physiological basis for understanding the potential ways in which sensory information is accessed, as well as ways in which the enhancement of afferent sensory signals may improve the control and perception of posture.

Inglis et al. (2002) reported differences in the magnitude of minimum detectable stimuli across a range of vibratory frequencies at 55 plantar surface locations on the foot. They found regional differences in the magnitude of the minimum detectable sensory stimulus across a wide range of vibration frequencies (25, 50, 25 and 400 Hz); these frequencies correspond to slow adapting type I and II and fast adapting type I and II (SAI, SAII, FAI and FAII, respectively) receptors. Individuals, both young and old, were able to identify vibratory stimuli of significantly smaller magnitudes at high frequencies compared to low frequencies. These findings suggest regional differences in the innervation of receptors such that different portions of the foot are tuned to meet specific postural demands. This 'tuning' was hypothesized in response to the observed differences in the distribution of stimuli detection between the hand and foot (Inglis et al., 2002; Johansson & Vallbo, 1983; Kennedy & Inglis, 2002) indicating that, while the sensory structures may be similar, there are differences in how the human body has evolved to allow for the regional tuning of sensory function. The differences in the psychophysical

identification of stimuli appears not to be entirely due to the distribution of sensory receptors, as the concentration of type I and type II receptors were not different across regions of the foot even though there are regional differences in the ability to detect cutaneous stimuli (Inglis et al., 2002). The manner in which the feet are 'tuned' for posture and gait remains unknown. Exploring how the pressure under the feet changes in different postures will allow for the assessment of the relation between pressure magnitudes and the detection of external stimuli.

The distribution of the cutaneous sensory receptors in the sole of the foot is relatively uniform (Figure 2.1), and this corresponds to an ability of the foot to

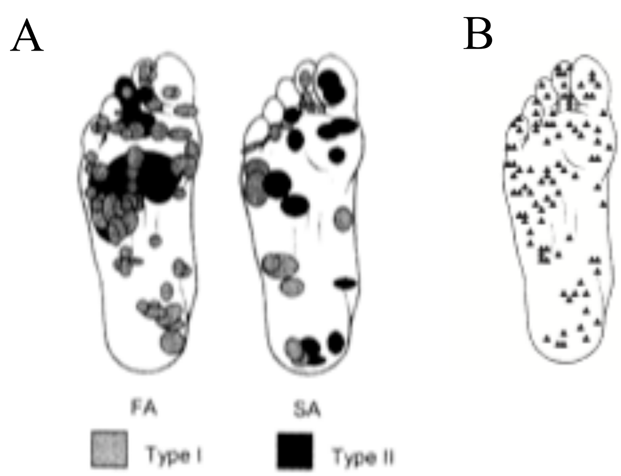

Figure 2.1: Sensory Receptor Distribution in Foot: A) receptive fields for each sensory receptor type (Inglis et al., 2002). B) total receptor distribution, all types. (Kennedy & Inglis, 2002)

detect external stimuli of a wide range of vibration frequencies: SA I, SA II, FA I, FA II (Johansson & Vallbo, 1983) have been shown to be most sensitive at 30, 50, 250 and 400 Hz, respectively (Johansson, Landstrom, & Lundstrom, 1982). The way in which the

information gathered from these receptors in the feet is incorporated into the control of posture remains unclear.

The location of the postural COP and distribution of plantar pressure are actively modulated under the feet. These constant adjustments may serve the purpose of providing meaningful fluctuations that allow for a contextualization of our body in the environment. The suggestion here is that we act in order to perceive and perceive in order to act (Gibson, 1962). It is likely that manipulating the pressure distribution under different portions of the feet will augment the postural COP fluctuations in a meaningful way, such that posture can be maintained (Riccio, 1993). In order to begin to understand the mechanisms behind how these postural fluctuations impact sensory detection, we propose here a study to address how changing the plantar pressure under the foot alters the ability to identify external stimuli.

2.2.1 Clinical Implications for Loss of Cutaneous Sensory Function

The loss of cutaneous sensory function is well documented in individuals with clinical conditions (e.g., multiple sclerosis, diabetes, aging, and stroke), and these same populations often exhibit reductions in postural control (Bonnet et al., 2009; Cattaneo & Jonsdottir, 2009; Cavanagh, Simoneau, & Ulbrecht, 1993; Geurts et al., 2005; Stelmach & Worringham, 1985). Postural control impairments may result in an increased rate of falls (Cattaneo et al., 2002; Matsuda et al., 2011; Peterson, Cho, von Koch, & Finlayson, 2008). Even in the absence of falls these disturbances in stability can impair quality of life in a significant way (Cattaneo & Jonsdottir, 2009).

Persons with multiple sclerosis (MS) rate balance control as one of the most important factors for maintaining a high quality of life (Heesen et al., 2008). Therefore it is important to develop techniques that can directly address the causes of balance loss. The information from this study may provide a framework for understanding how sensation deficits directly impact postural control.

2.3 Postural Control

There is a significant body of work in the area of posturography that seeks to identify how clinical disorders impair the control of upright standing. Traditionally, techniques identify postural control as being clinically impaired if measures of the postural COP (e.g., path length, ellipse area, velocity and acceleration) are altered compared to healthy populations. These measures have in many cases been useful for identifying disability, but they lack the ability to distinguish adaptations that are functional from those that are not. Recently, techniques have been developed which examine fluctuations in the postural COP time series in order to identify how complexity of the signal changes in a manner that is consistent with the theoretical underpinnings of the “loss of complexity” hypothesis (Goldberger, Peng, & Lipsitz, 2002; Lipsitz, 2002; Lipsitz & Goldberger, 1992). Studies examining changes in physiologic complexity associated with aging and disease indicate that biological signals, such as the postural COP, can indicate disturbances in the regulation of biological processes Impairment can be characterized by a loss in the functional degrees of freedom (Fig 2.2). The functional impact of reduced physiological complexity is an impaired ability of a person to adapt to challenges to the system. For postural control this means that gaining insight into the

underlying COP patterns, through techniques like entropy analysis, can be more sensitive to changes in system health. These same techniques that are able to distinguish between functional and non-functional variability may provide insight into how disruptions in physiological processes impact balance control.

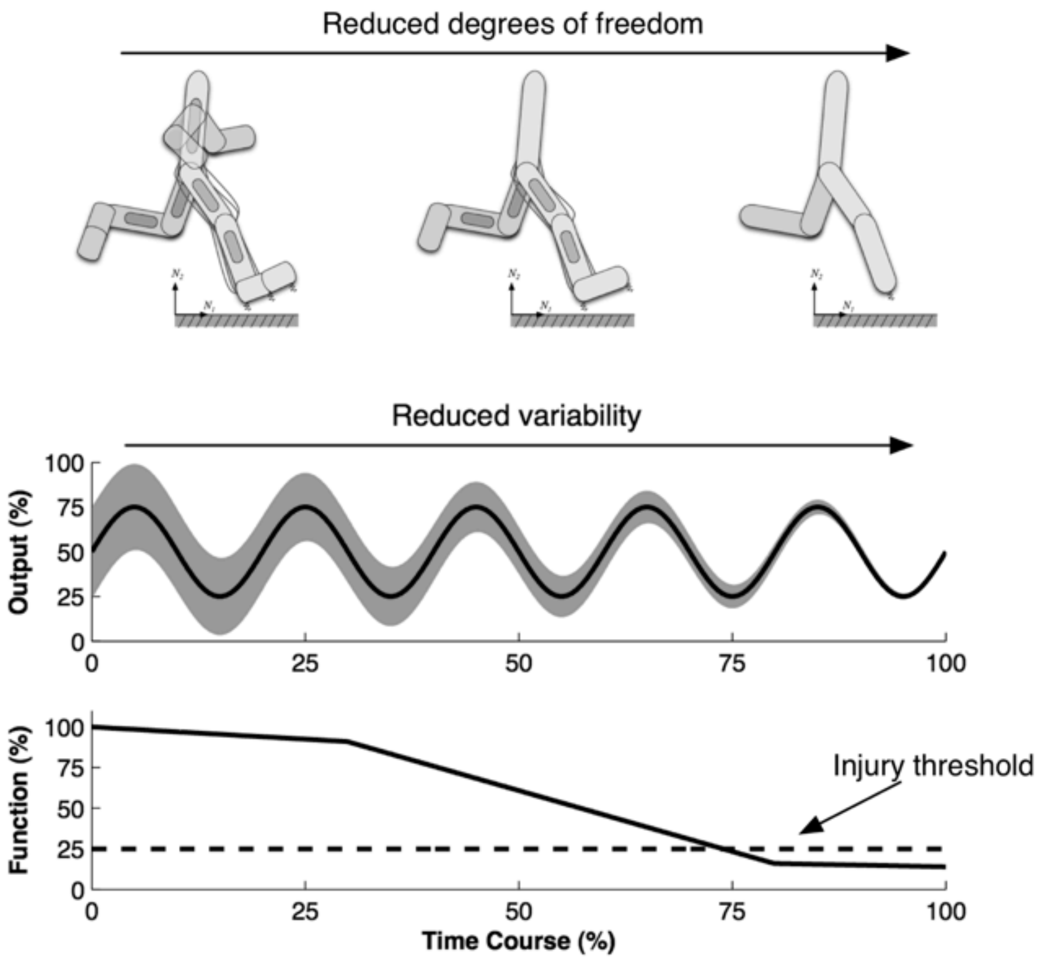

Figure 2.2: Loss of Complexity Hypothesis: (Van Emmerik et al., 2013)

2.3.1 Quantifying Functional Variability in Posture

Many different techniques have been used in the quantification of postural control, but those which approach this problem from an ecological and dynamical

systems perspectives examine how degrees of freedom, formed from functional neuromuscular units, self-organize in order to produce adaptable responses to postural challenges (Costa et al., 2005; Hausdorff, 2005; Riccio, 1993; Turvey, 1990; Turvey, Fitch, & Tuller, 1982; Van Emmerik et al., 2013). An important focus in this research is to discuss how coordinative variability serves a functional role in the performance of postural tasks. Methods have been developed which identify variability of movement, including the uncontrolled manifold (Scholz & Schoner, 1999) and entropy techniques (Costa et al., 2002).These techniques allow for an assessment of functional versus non-function variability, in particular entropy techniques have been demonstrated to provide insight to how physiological processes unfold at a number of timescales. These entropy techniques are based on information and thermodynamic theory and examine changes in point-to-point fluctuations in time series. These methods have demonstrated improved sensitivity to changes in postural control between clinical outcome measures in adolescent scoliosis patients (Gruber et al., 2011), and between those with mild-to-moderate multiple sclerosis who exhibit little clinical movement disorder and healthy controls (Busa, et al., unpublished data).

2.3.1.1 Loss of Complexity Hypothesis

The role of physiological variability has recently received a large amount of attention in the literature (Gruber et al., 2011; Kang et al., 2009; Lipsitz, 2002; Lipsitz & Goldberger, 1992; Liu et al., 2002; Manor et al., 2010; Van Emmerik et al., 2013). The manner in which functional variability contributes to the health of a system is nicely outlined in the "loss of complexity" hypothesis (Figure 2.2) (Goldberger et al., 2002;

Lipsitz, 2002; Lipsitz & Goldberger, 1992). This hypothesis states that when a system's degrees of freedom are reduced due to disease or aging, decreases are observed in the variability of motor patterns and this is a pathway to disability (Goldberger et al., 2002; Van Emmerik et al., 2013).

Turvey and colleagues (1990; 1982) have identified that variation in the manner in which individuals accomplish an invariant task can serve as a way to understand functional variability, where by the body is able to use a variety of combinations of functional units to keep task space dynamics invariant. Movements are coordinated over many temporal and spatial scales, integrating system elements as small as the motor unit and as large as whole organism multisegment movements (Van Emmerik et al., 2013).

There is an expanding body of literature that explores how having redundant degrees of freedom in biological systems provides for a rich manifold of movements that are characterized by variability (Van Emmerik et al., 2013). The dynamical systems view of variability acknowledges that patterns of behavior functionally emerge as adaptations to environmental influences; this is in contrast to traditional views of variability where these same fluctuations are viewed as noise in the system. The degradation of the fundamental units (e.g., motor units and muscles) associated with aging and disease can lead to reductions in functional couplings. A number of studies have demonstrated how disease impacts the complexity of heart, brain and locomotor function (Costa et al., 2002, 2005; Glass, 2001; Lipsitz, 2002), consistently reporting that pathologies can be characterized by reduced complexity in physiological processes. Techniques that are able to identify features of physiological signals that are indicative of functional variability

and are both reliable and sensitive to identifying changes in health states, provide an ideal way to examine how changes in sensory function impacts postural control.

2.3.1.2 Entropy Techniques for Quantifying System Complexity

The entropy family of statistics that have begun to gain a foothold in movement science are broadly positioned to assess the complexity of time series data. Currently there are two entropy measures used to assess complexity in postural control, approximate entropy (Eqn. 2.1) (Pincus, 1991) and sample entropy (Eqn. 2.2) (Richman & Moorman 2000), both of which are estimates of Kolmogorov Entropy (Eqn. 2.3)

$$ApproximateEntropy = \phi^{m}(r) - \phi^{m+1}(r) \quad \text{Eqn. 2.1}$$

$$SampleEntropy = -\ln\frac{\phi_{m+1}(r)}{\phi_{m}(r)} \quad \text{Eqn. 2.2}$$

$$KolmogorovEntropy = \lim_{r\to 0}\lim_{m\to\infty}\lim_{N\to\infty}[\phi^{m}(r) - \phi^{m+1}(r)] \quad \text{Eqn. 2.3}$$

where r is radius of similarity, m is the window of comparison, and Φ is probability that two points are the m points apart fall within a radius of r. While both of these algorithms aim to assess the complexity of biological signals, Richman and Moorman (2000) highlight that self-matching bias that can arise in the approximate entropy algorithm and advocate for the sample entropy method as a more robust, reliable way to assess point-to-point fluctuations in biological processes. Sample entropy has since been expanded into multiscale (Costa et al., 2002) and control (Bollt, Skufca, & McGregor, 2009) entropy techniques which explore complexity of biological systems at multiple time scales and under non-stationary processes, respectively. Multiscale entropy has been used to

evaluate the “loss of complexity hypothesis” (Lipsitz, 2002; Lipsitz & Goldberger, 1992), where loss of complexity, quantified as a decrease in entropy at many time scales, is a pathway to disability or injury.

Entropy techniques examine time series for how point-to-point fluctuations vary, with increased variation being indicative of greater systemic redundancy, allowing for a greater solution set of responses. This increased solution set indicates that a system has a less rigid control structure, indicating a degree of functional variability. Multiscale entropy was developed in order to examine how the complexity of physiological processes change over many time scales. This provides important information as to how physiological processes are regulated over the relevant time scales at which the neuromuscular processes occur.

Sample, multiscale, and control entropy are all variations of the sample entropy technique to calculate the complexity of a time series. The sample algorithm (Eqn.2.2) calculates the negative algorithm of a conditional probability that repeated patterns of length m are similar to those of length $m+1$. Subtle changes to the sample entropy algorithm allow for the understanding of complexity at one time scale (Sample Entropy) (Richman & Moorman 2000), many time scales (Multiscale Entropy) (Costa et al., 2002), or one time scale with non-stationary data (Control Entropy) (Bollt et al., 2009).

Entropy techniques have been applied to the study of postural control and gait for the examination of how individuals with clinical disorders differ in the complexity of control processes (Costa et al., 2007; Gruber et al., 2011; Kaipust, Huisinga, Filipi, & Stergiou, 2012; Kang et al., 2009; Manor et al., 2010; McGregor, Busa, Skufca, Yaggie, & Bollt, 2009). These studies have consistently reported lower entropy values in

populations that exhibit clinical impairment. Few exceptions to this have been reported and those that do have all used the approximate entropy method (Cavanaugh, Mercer, & Stergiou, 2007; Georgoulis, Moraiti, Ristanis, & Stergiou, 2006). However this same group has recently advocated for the use of sample entropy, especially when using short time series (Yentes et al., 2013).

Studies implementing multiscale entropy have demonstrated that the area under the sample entropy vs. time scale curve, the complexity index (C_i), is a metric that allows for the examination of physiological complexity across many time scales (Costa et al., 2005; Costa, Peng, & Goldberger, 2008; Gruber et al., 2011) (for an example see Figure 2.3). The use of the complexity index has been shown to be more sensitive to changes in distinguishing between clinical subgroups than other measures of postural control (Gruber et al., 2011), indicating that changes in the postural fluctuations may precede observable changes in measures which observe more coarse-grained processes, such as COP velocity, path length or sway area. Others have also reported reduced complexity in the postural control among older individuals (Costa et al., 2007; Kang et al., 2009; Manor et al., 2010).

2.3.2 Perception of Posture

Beyond the control of posture, individuals' perception of body orientation can be impacted by sensory function. Having a high degree of complexity in the postural COP position as well as an accurate perception in body orientation should provide for the greatest potential for successful responses to postural challenges. As this will allow

individuals to produce a wide manifold of responses that can be correctly selected for the configuration the body is in.

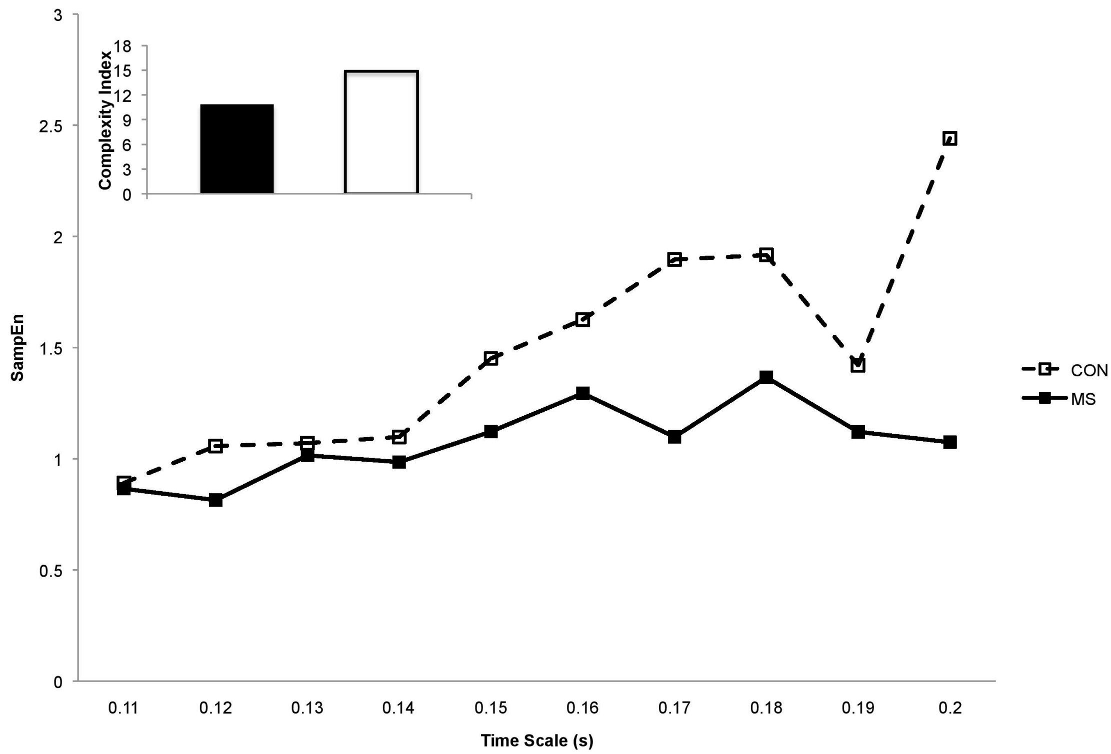

Figure 2.3: MSE Plot: Example of Multiscale Entropy of medial-lateral COP position for two age, gender, height, and weight matched individuals, one with and one without MS (CON). Sample entropy vs. time scale, complexity index (inset).

Information from vestibular, visual and touch sensory structures are dynamically integrated to influence the control of posture (Oie, Kiemel, & Jeka, 2002; Polastri et al., 2012; Stoffregen & Bardy, 2001). The effective integration of these information sources is necessary to accurately perceive body orientation. When the number of sensory processes is limited, the ability to recreate postures is impaired relative to conditions where more sensory information is present (Fujiwara, Asai, Kiyota, & Mammadova, 2010; Fujiwara et al., 2003).

Fujiwara et al. (2010) reported that standing postures close to the quiet standing position are more difficult to reproduce than postures that place the COP closer to the anterior/posterior boundaries of the feet. They suggested that additional stretch in the tissue that spans the ankle enhances the ability to accurately perceive body position; inferring that postures evoking more neutral activity in these tissues would receive sufficiently reliable information to recreate these more extreme postures. Furthermore, the same group has reported that cooling the soles of the feet impairs the ability to recreate reference positions, indicating that reducing reliable sources of sensory information can increase degradation of postural awareness (Fujiwara et al., 2003). These findings support the choices of the reference postures used in this dissertation. Additionally the findings that cooling of the feet cause additional impairments to the ability to recreate postural configurations, supports the decision to use cooling of the feet as a means to impair the perception of posture. However it should be noted that Fujiwara and colleagues only explored this in the context of an extreme temperature reduction (1 degree Celsius skin temperature). The approach in this dissertation expands on this limited understanding to gaining insight as to how acute changes in sensory function, in clinically relevant range, impact the perception of posture, and whether or not SR can improve this performance.

2.4 Integration of Multisensory Function

The control of posture is not only influenced by cutaneous sensation, but results from the integration of many sources, including visual, vestibular, cutaneous, and proprioceptive sensory information. The manner in which these different sources of

sensory information are integrated has been explored in a number of studies, which examine how postural fluctuations are influenced by changes in tactile and visual information (Fujiwara et al., 2003; Jeka et al., 2000; Kiemel et al., 2002; Polastri et al., 2012).

Jeka and colleagues have undertaken a series of experiments that seek to gain an understanding of how vision and touch influence postural control (Allison, Kiemel, & Jeka, 2006; Jeka et al., 2000; Oie et al., 2002; Polastri et al., 2012). Previous to this work it was assumed that sensory inputs were linearly additive, but early on Jeka's work demonstrated this was not the case (Kiemel et al., 2002). Rather, it appears that sensory processes interact in a non-linear way. That is, when one mode of sensory information becomes unreliable, the weighting of specific sources of sensory information is dynamically shifted to more reliable sources of information. This concept was expanded in an attempt to further understand the factors that influence the inter- and intramodal dynamics of sensory reweighting (Polastri et al., 2012). The manner in which reweighting occurs remains uncertain; however, what is clear is that compensatory actions are dynamic and ever changing.

The manner in which a single sensory modality is used within the context of a multisensory system appears to be based on reliability. That is, when one sensory modality experiences dysfunction or becomes unreliable, weighting is shifted to more reliable or available sources (Oie et al., 2002). This reweighting is exemplified in work that has identified an emphasis on visual information for the control of balance among older adults who exhibit impairments in somatosensory function (Sundermier, Woollacott, Jensen, & Moore, 1996; Wade, Lindquist, Taylor, & Treat-Jacobson, 1995).

However, this ‘visual dependence’ is not apparent in participants who do not exhibit deficits in peripheral sensation (Allison et al., 2006), suggesting that sensory reweighting observed in those with somatosensory loss may be due more to specific sensory impairments than age related change. This work suggests that among compensatory sensory processes it is necessary to remove sources of redundancy in order to assess the function of a specific sensory modality. The resultant changes in outcome variable can then be attributed to degradations of the sensory mode in question, in contrast to a dynamic reweighting to more reliable sources of sensory information.

Stoffregen and Bardy (2001) discuss an alternate theory of how multiple sources of sensory information are integrated. They view perception as a more dynamic process without redundancy in perceptual systems. This theory is summarized in their three hypotheses: “1) that there is an ambiguous relation between ambient energy arrays and physical reality, 2) that there is a unique relation between individual energy arrays and physical reality, and 3) that there is a redundant but unambiguous relation, within or across arrays, between energy arrays and physical reality.” The examination of experiments that view these different contexts for sensory and action integration forms an argument that there is no clear basis for the assumption that perception is carried out by a clearly defined set of perceptual systems. Rather, they point to perception as an accumulation of sensory information across sensory modalities. While this approach does not directly address how sensory information is integrated, it does indicate that by limiting specific sources of sensory information would place reliance on the available perceptual structures.

Stoffregen and Bardy (2001) point to establishing protocols similar to those implemented by Jeka and colleagues that have been used to explore how different sensory modalities contribute to the control of physical outcomes. While the specific methods are not the same as those proposed in this dissertation, that does not discount the importance of the information that this set of experiments can provide.

2.5 Cooling of the Skin Alters Sensory Function and Stimulus Detection

There are many ways in which sensory function can be altered (cooling, pharmacological, and pressure) in order to gain understanding of how the information from a particular sensory source impacts the control of posture and environmental interaction. While all of these different techniques are effective at disrupting neural function, cooling has been shown to exhibit consistent changes in both neural function and the ability to detect sensory stimuli (Lowrey, Strzalkowski, & Bent, 2013). Cooling of the extremities has demonstrated decreases in the ability to detect external stimuli (Fujiwara et al., 2003; Weitz, 1941, 1942) and these decreases are associated with impairments in the ability to perceive postural orientation (Fujiwara et al., 2003) and postural control (Billot, Handrigan, Simoneau, Corbeil, & Teasdale, 2013).

Fujiwara et al. (2003) examined how cooling the plantar surface of the feet influences the ability to perceive postural orientation through a body repositioning task. The task in this experiment was for participants to recreate body orientations through ankle joint rotations that placed the postural COP position at specific reference locations corresponding to percentages of foot length. The reference positions ranged from 20-80% of the foot length, in 10% increments (Figure 2.4), with normal quiet standing occurring

at an average of 45% of foot length. The outcome of this study revealed that, independent of foot cooling, reference positions at 40%, 50% and 60% of foot length resulted in significantly greater absolute errors in repositioning the postural COP than more extreme leans (i.e., 20, 30, 70, and 80% of foot length). Errors were also greater in the cooled condition at these same postures. Additionally, in the cooled condition errors occurred significantly further forward in the 50 and 60% reference positions. Fujiwara et al. (2010) attributed the observed differences in the ability to recreate postures near that of the quiet standing center of pressure position were due to a lack of stretch in the sensory receptors spanning the ankle. This however cannot be confirmed, as there is a lack of experimental data as to how sensory information from musculoskeletal structures spanning the ankle joint influences the perception of body orientation.

Billot et al. (2013) suggested that the changes in control of posture are mediated through reductions in sensory function. However, these reductions in control, measured as increased postural COP velocity and decreased EMG activity in muscles of the lower leg, were short term and control was restored to pre-cooling after a single trial. The authors suggest that the return to normal postural control is because sensory reliance is shifted toward more reliable sensory modalities in the presence of temperature-mediated impairment in cutaneous sensation. This reweighting highlights the importance of limiting redundancy when attempting to evaluate the capacity of one sensory modality.

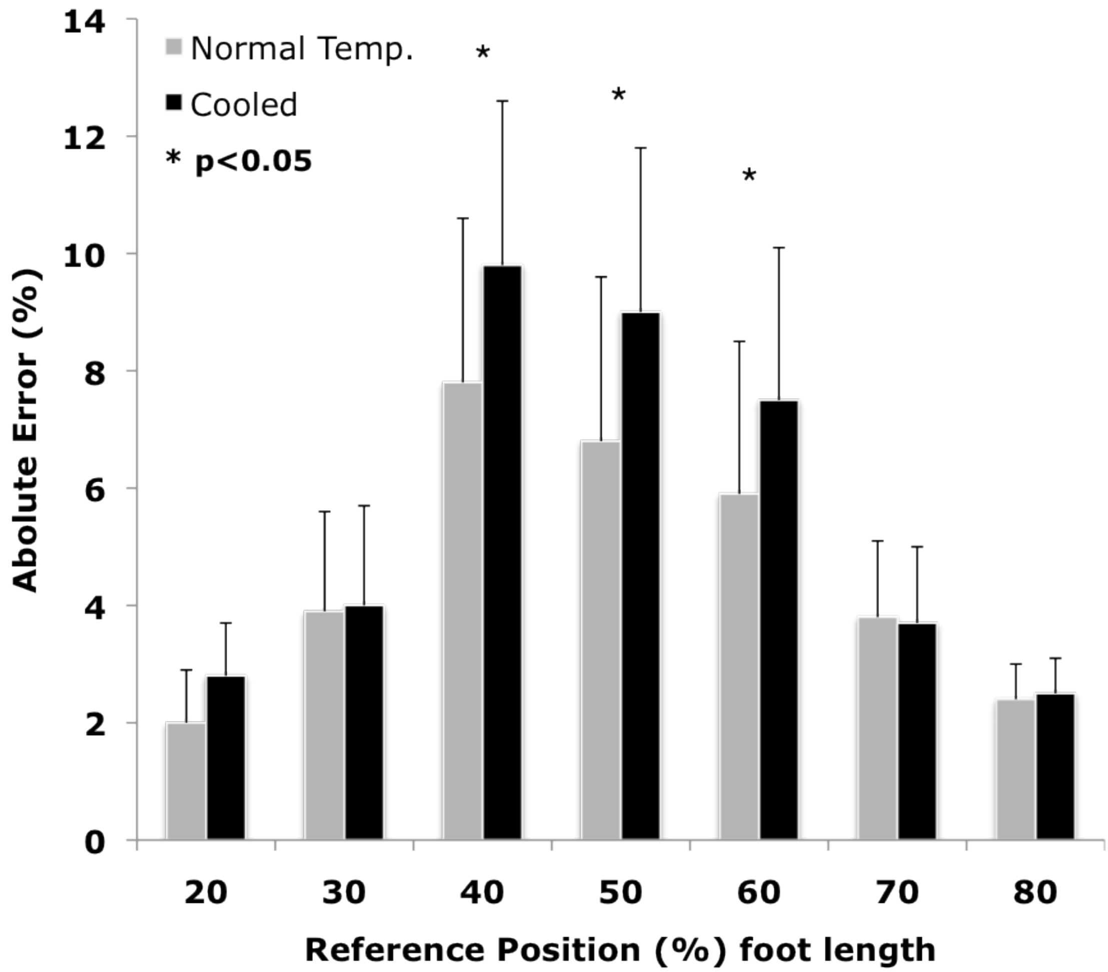

Figure 2.4: Error in Postural Repositioning: Increases in positioning error with cooling (open bars) compared to normal condition (black bars) with 0% and 100% being the posterior and anterior boundaries of the feet, respectively (Fujiwara et al., 2003).

2.6 Methods for Improving Postural Control

Decrements in postural control are observed in many populations, e.g., the elderly (Illing et al., 2010; Priplata et al., 2003; Sihvonen et al., 2004), people with diabetes (Bonnet et al., 2009; Priplata et al., 2006), people suffering from MS (Chung et al., 2008; Fjeldstad et al., 2009; Martin et al., 2006; Van Emmerik et al., 2010), stroke patients (Geurts et al., 2005; Priplata et al., 2006; Rougier & Boudrahem, 2010), and cerebral palsy sufferers (Rose et al., 2002). Attempts have been made to address these deficits

using a variety of training and bio-medical interventions: balance and resistance training, biofeedback training in a variety of forms, vibration intervention (locally and whole body), and noise-based aids that utilize stochastic resonance behavior. The mechanism by which each of these methods addresses postural control is different. The focus of this section is to discuss the use of these interventions and aids, evaluate their effects, and identify a method that is best able to fundamentally improve postural control when the ability to detect external stimuli is impaired.

2.6.1 Balance and Resistance Training

Balance and resistance training rely on the same proposed mechanism: progressive overload. Progressive overload works on the principle that people are effectively able to increase skill level an appreciable amount by making continuous small improvements, above their current abilities (Kraemer et al., 2002). Balance and resistance progressive overload paradigms have been used as interventions for the improvement of postural control.

Balance training studies have investigated a variety of paradigms, including single (Granacher, Muehlbauer, Zahner, Gollhofer, & Kressig, 2011; Silsupadol, Shumway-Cook, et al., 2009; Silsupadol, Siu, Shumway-Cook, & Woollacott, 2006) and multidimensional (Granacher et al., 2011; Shumway-Cook, Gruber, Baldwin, & Liao, 1997; Silsupadol, Shumway-Cook, et al., 2009; Silsupadol et al., 2006) approaches. Singularly focused approaches utilize a series of progressively more difficult postures in order to achieve a more stable pattern of balance. Multidimensional approaches are instituted in a number of ways, including dual-task methodologies as well as combining

both strength and balance training. In dual-task training participants simultaneously perform both a balance and a cognitive task, where priority between the tasks can be either researcher assigned or unspecified (Silsupadol, Shumway-Cook, et al., 2009; Silsupadol et al., 2006). Other methods utilize strength and balance training concurrently, often with subject-specific interventions to overcome postural deficits (Shumway-Cook et al., 1997).

Studies comparing the effects of single and dual-task performance have reported that both methodologies are effective at addressing postural control when the tasks used for evaluation were similar to those used in the intervention (Simeonov et al., 2011; Thompson, Belanger, & Fung, 2011). Only dual-task training, however, has reported improvement in novel tasks (Silsupadol, Shumway-Cook, et al., 2009; Silsupadol et al., 2006). Gait velocity and normalized stride length were improved in both single and dual-task gait training, while more stable gait patterns (reduced frontal plane ankle – center of mass angle) were only reported in dual-task gait training (Silsupadol, Lugade, et al., 2009). A review of 35 single and dual-task balance training interventions (Granacher et al., 2011) rates the outcomes of these studies as having an average Physiotherapy Evidence Database score of 4.8 (range 0-10 with 10 being best) ("PEDro scale," 2010). Dual-task paradigms were reported as being more effective at inducing acute and long-term balance improvements ("PEDro scale," 2010). Overall, it appears that balance-training methodologies are task specific, and even dual-task training, while more effective, cannot overcome this limitation.

The use of resistance training has also been implemented for the purpose of improving postural control. Orr recently completed a review that synthesized the results

of studies that included measures of muscular strength or power and balance performance in older adults. The purpose of the review was to identify links between muscular performance and postural control (Orr, 2010). The review identified a possible mechanism for reduced balance performance being the loss of α-motorneurons, the associated decreases in neural conduction velocity, and increased muscle activation latencies (Orr, 2010). Increasing muscular strength and power may be key components to improving postural control deficits, as it could allow for rapid and appropriate response to challenges to balance. The efficacy of resistance training is reliant on the ability to transfer improvements in strength and power to the control of posture; the capability to do so is unknown at this time (Barry & Carson, 2004).

The hypothesis that leg power is more important than strength is supported by a report that elderly women with a history of falls had 24% less powerful leg muscles than non-fallers, while demonstrating similar leg strength (Skelton, Kennedy, & Rutherford, 2002). Reduced power in the knee extensors has also been associated with increased postural COP variability in multiple sclerosis patients (Chung et al., 2008). These results indicate that the role of muscular power may be more important than strength alone, however training interventions, typically, do not make this distinction; therefore the mechanism by which postural control improves is difficult to identify. A meta-analysis revealed moderate improvement in functional outcomes for power training interventions compared to strength training in elderly persons (Tschopp, Sattelmayer, & Hilfiker, 2011).

Increases in lower extremity power should be a focus of future interventions to improve postural control, as this may be the mechanism by which resistance training

could be most effective. A review of progressive resistance training programs reported improvements in postural control in only 22% of included studies (Orr, Raymond, & Fiatarone Singh, 2008), suggesting resistance training alone may not provide an adequate solution for improving balance. It is unknown whether resistance training alone, either strength or power focused, can provide significant improvements in postural control, or if this training modality coupled with more balance focused techniques would provide the best outcomes.

2.6.2 Biofeedback Training

Sensory biofeedback training utilizes biological signals to provide additional sensory information to a person performing a task. The utilization of this supplemental sensory input, if successful, allows for people with one particular sensory deficit to overcome it by relying more heavily on information gathered from other senses. The effects of a variety of biofeedback modalities have been examined, including visual (Barclay-Goddard, Stevenson, Poluha, Moffatt, & Taback, 2004; Bisson, Contant, Sveistrup, & Lajoie, 2007; Geiger, Allen, O'Keefe, & Hicks, 2001; Hatzitaki, Voudouris, Nikodelis, & Amiridis, 2009; Rougier & Boudrahem, 2010; Sihvonen et al., 2004; Srivastava, Taly, Gupta, Kumar, & Murali, 2009; Van Peppen, Kortsmit, Lindeman, & Kwakkel, 2006; Winstein, Gardner, McNeal, Barto, & Nicholson, 1989), tactile (Bittar & Barros Cde, 2011; Dozza, Wall, Peterka, Chiari, & Horak, 2007; Sienko, Vichare, Balkwill, & Wall, 2010; Tino, Carvalho, Preto, & McConville, 2011; Wall, 2010; Wall, Wrisley, & Statler, 2009), and auditory (Dozza, Chiari, Peterka, Wall, & Horak, 2011), with some studies coupling multiple feedback sources (Barclay-Goddard et al., 2004;

Dozza et al., 2011). These studies have analyzed a wide variety of outcome measures, including; postural COP and center-of-mass (COM) dynamics during non-moving postures (Barclay-Goddard et al., 2004; Bittar & Barros Cde, 2011; Hatzitaki et al., 2009; Sienko et al., 2010; Sihvonen et al., 2004) and dynamic activities (Bisson et al., 2007; Hatzitaki et al., 2009; Sihvonen et al., 2004), clinical outcome measures (e.g., Berg Balance Scale, Dynamic Gait Index, Community Balance and Mobility Scale) (Barclay-Goddard et al., 2004; Bisson et al., 2007; Geiger et al., 2001; Srivastava et al., 2009; Wall et al., 2009; Winstein et al., 1989), postural symmetry (Barclay-Goddard et al., 2004; Van Peppen et al., 2006; Winstein et al., 1989), stride parameters (Van Peppen et al., 2006; Winstein et al., 1989), gait symmetry (Van Peppen et al., 2006; Winstein et al., 1989), and upper body responses to postural challenges (Hatzitaki et al., 2009).

The use of different experimental methods has made results difficult to generalize. Different feedback techniques have equivocal outcomes across a range of populations: young, old, hemi-paretic stroke patients, those with central imbalance, and elderly individuals with fall history. There are some examples of improved postural COP and COM dynamics in static postural tasks (Hatzitaki et al., 2009; Sienko et al., 2010), while other studies report no improvement or no change in results from balance or resistance training (Barclay-Goddard et al., 2004; Bittar & Barros Cde, 2011; Van Peppen et al., 2006). During dynamic tasks there are some examples of postural improvements (Bisson et al., 2007; Hatzitaki et al., 2009; Sihvonen et al., 2004) and some improvements in upper-body control (Hatzitaki et al., 2009). Many post-training assessments reported no difference or minimal improvement compared to resistance and balance task training

(Bisson et al., 2007; Sihvonen et al., 2004), making differentiating between improvements in postural control and task acquisition difficult.

When postural symmetry (50/50 weight balance between feet) is assessed in hemi-paretic stroke patients, equivocal results are reported, with some studies reporting more symmetrical weighting of the feet (Barclay-Goddard et al., 2004; Winstein et al., 1989) while others report no change compared to those not receiving feedback (Van Peppen et al., 2006). Biofeedback has inconsistent results for the improvement of gait parameters, with some reporting improvements in gait speed and stride length (Van Peppen et al., 2006; Winstein et al., 1989) while simultaneously not demonstrating improvements in gait asymmetry (Van Peppen et al., 2006; Winstein et al., 1989). Improvement in clinical outcome measures is also inconsistent. In response to biofeedback intervention, some studies report improvement (Sihvonen et al., 2004; Wall et al., 2009), while a greater number report no clinical change or no difference as compared to balance and resistance interventions (Barclay-Goddard et al., 2004; Bisson et al., 2007; Geiger et al., 2001; Srivastava et al., 2009).

These results illustrate that the efficacy of biofeedback training for the improvement of postural control is still not fully determined. There are studies that demonstrate the usefulness of biofeedback, as well as those that report no differences compared to balance or resistance training. It is possible that biofeedback interventions could be improved with the implementation of resistance training focusing on muscular power. This type of paradigm may have the benefit of improving the perception of balance control through feedback as well as improving the ability to quickly respond to balance disturbance through increasing muscular power. There are no studies combining

power and biofeedback training at this point in time, and the efficacy of this type of combined intervention should be explored, as it may provide better outcomes than resistance or biofeedback training alone.

2.6.3 Vibration

Vibration of the whole body (Arias, Chouza, Vivas, & Cudeiro, 2009; Carlucci, Mazza, & Cappozzo, 2010; Rees, Murphy, & Watsford, 2009; Spiliopoulou, Amiridis, Tsigganos, Economides, & Kellis, 2010) or individual body segments (Simeonov et al., 2011; Thompson et al., 2011) as well as a source of postural feedback for the purpose of enhancing postural control (Wall, 2010; Wall et al., 2009). The proposed mechanism by which vibration would be an effective intervention for improving posture is that after receiving a vibration stimulus, muscle spindle Ia afferents are in a heightened state of sensation, much as if the muscle had been stretched (Thompson et al., 2011), and deliver sensory information at an enhanced rate (Burke, Hagbarth, Lofstedt, & Wallin, 1976; Thompson et al., 2011). As a source of feedback, suprasensory vibrations have been applied to the trunk (Dozza et al., 2007; Wall, 2010; Wall et al., 2009) and extremities (Rupert, 2000; Tino et al., 2011) to deliver supplemental information regarding body position.

Whole body vibration is generally applied via a vibrating stimulus to the feet during standing posture (Rees et al., 2009). The effects of whole body vibration are mixed, with some studies reporting some postural benefits (Rees et al., 2009; Spiliopoulou et al., 2010), others reporting placebo effects (Arias et al., 2009) and still others reporting no lasting effects (Carlucci et al., 2010), i.e., there is no retention of

balance performance apart from directly after vibratory stimulation. Studies reporting improvements in postural control indicate that the greatest benefit due to whole body vibration intervention was observed in participants with the poorest initial balance (Rees et al., 2009; Spiliopoulou et al., 2010). These improvements may be due to improvements in the power of the knee extensors, observed post-vibration (Spiliopoulou et al., 2010). Whole body vibration training is not without risk, as side effects including faintness, nausea, skin erythema, edema and pain have been reported (Crewther, Cronin, & Keogh, 2004; Rittweger, Beller, & Felsenberg, 2000; Rubin et al., 2003).

When vibration is applied to the feet at a supersensory threshold level it has been reported that sway of the upper body increases in both young and elderly individuals; however vibration applied below the sensory threshold did not demonstrate consistent effects on postural control (Simeonov et al., 2011). However, researchers suggested that imprecise sensory perception threshold identification might be the cause of this finding, as some participants did improve postural control (Simeonov et al., 2011). Thompson et al. (2011) examined the effect of postural control strategies in the presence of plantar surface and achilles tendon vibration and reported that the presence of the mechanical stimulus resulted in increased knee and hip flexion and trunk extension in the control of both quiet and perturbed stance. The alteration in control strategy suggests that the central nervous system utilizes somatosensory information from the Ia afferents to adjust postural responses (Thompson et al., 2011). The sensitivity of postural control to vibration parameters (i.e. amplitude and frequency) is not well documented at this time; further understanding of how vibration impacts the sensory structures of the feet needs to be explored to identify the consequences of using different vibration levels.

Vibration has also been used as a source of tactile feedback for the purpose of improving postural control. Several studies have examined the effect of vibrotactile feedback and how it relates to control of static balance and gait (Dozza et al., 2007; Rupert, 2000; Wall, 2010; Wall et al., 2009), and have developed new devices which can be worn in real-world conditions (Tino et al., 2011). Studies examining both older individuals with a history of falls and individuals with vestibular impairments report significant improvements in dynamic gait index (Wall, 2010; Wall et al., 2009) when wearing vibrotactile feedback devices compared to without any aid. However, none of these studies address how vibration, intended as a feedback source, may stimulate muscle activation at the point of stimulus, making it impossible to determine if the changes in posture are due to the feedback or enhanced muscle activation. It is possible that this type of aid may provide the dual effect of sensory feedback to postural disturbances as well as enhancing muscle activation; further work is necessary to identify whether this is the case.

2.6.4 Stochastic Resonance

Stochastic Resonance (SR) is a phenomenon by which the transmission of a non-linear signal is enhanced by the presence of noise. The concept of SR has its roots in the field of physics (Benzi et al., 1981), and its first application was in the study of climate fluctuations and their underlying causes (Benzi, Parisi, Sutera, & Vulpiani, 1982; Nicolis, 1982). In simple climate models, the addition of white noise (that which has equal power spectrum within a fixed bandwidth) permits the pattern of climate fluctuations to be reproduced, with appropriate spikes in climate changes from one period of stability to

another (Benzi et al., 1982). These changes were not reproduced by models that did not have noise added (Benzi et al., 1982; Nicolis, 1982). Application of SR to human systems began in the mid-1990's (Collins, Chow, & Imhoff, 1995a; Collins et al., 1995b), and has been an effective way to improve neural information flow (Collins, Imhoff, & Grigg, 1996a, 1997). This research has been extended to examine how sensory information can be enhanced by the addition of subsensory tactile noise to allow people to overcome somatosensory deficits (Collins et al., 2003; Costa et al., 2007; Dhruv, Niemi, Harry, Lipsitz, & Collins, 2002; Galica et al., 2009; Khaodhiar et al., 2003; Magalhaes & Kohn, 2011a; Priplata et al., 2002; K. A. Richardson, Imhoff, Grigg, & Collins, 1998).

Application of SR signals has demonstrated enhanced detection of subthreshold signals, and has been systematically examined in both simple (Collins et al., 1995a) and complex (Collins et al., 1995b) artificial neural networks. It appears that the frequency content of subsensory noise added to a neural network does not need to be tuned. Variability between the individual neurons within a complex system confers the ability to utilize a wide variety of noise frequencies (Collins et al., 1995b), and these systems are not as sensitive to specific noise frequencies as models of one neuron (Collins et al., 1995a, 1995b). However, SR signal amplitudes should be tuned as to increase the likelihood of neural activation for subsensory stimuli, without resulting in the signal becoming suprathreshold which may impair the ability to identify the correct stimulus (Collins et al., 1995b), thus advocating for an optimal noise amplitude level (Chow, Imhoff, & Collins, 1998) (Figure 1.3). Noise amplitude is important, as it needs to be large enough to induce negative masking within the neural network. Negative masking is a phenomenon through which detection of a weak signal can be enhanced by the presence

of another signal (Priplata et al., 2002). SR behavior has demonstrated the ability to enhance tactile sensation without *a priori* knowledge of the external stimulus (Priplata et al., 2002); rather, the imparted noise need only be tuned to the naturally occurring sensory threshold, such that it allows for optimal sensory activation.

SR signals have been applied to neural activity (Collins et al., 1996a), and this work indicates that the addition of noise to *in vitro* SA1 afferent fibers in rats can enhance the ability of the detection of weak stimuli. The presence of SR behavior in rat cutaneous mechanoreceptors provides evidence that SR exits in biological systems and may be an effective way to enhance tactile sensation in humans (Collins et al., 1996a). The presence of SR behavior in humans has been confirmed by several additional which examined sensory and postural enhancement in when SR signals are applied (Collins, Imhoff, & Grigg, 1996b; Dhruv et al., 2002; K. A. Richardson et al., 1998; Simonotto et al., 1997).

Enhancement of sensation through the addition of noise has been well characterized in the tactile realm (Collins et al., 1997; Dhruv et al., 2002; Gravelle et al., 2002; Khaodhiar et al., 2003; Kimura, Kouzaki, Masani, & Moritani, 2012; Liu et al., 2002; Magalhaes & Kohn, 2011b; Priplata et al., 2003; Priplata et al., 2006; K. A. Richardson et al., 1998). Additional work has been done in vision and hearing, and for a thorough review see Moss et al. (2004). To stay within the scope of the experiments proposed here we will focus on the application of SR to tactile sensation. Liu et al. (2002) examined several populations which typically exhibit diminished tactile sensation and reported that healthy older individuals, stroke patients and those suffering with diabetic neuropathy all exhibited improved tactile sensation when subsensory white noise was

applied to the feet. When noise was applied at 90% of sensory threshold level, detection improved in both the hands (30% in older, 16% in stroke and 34% in diabetic neuropathy), and feet (31% diabetic neuropathy). Trial to trial variation was noted, however there appeared to be no systematic adaptation to the noise application, i.e., the first trial was no more or less successful than the last over the course of the two-hour examination period (Liu et al., 2002). Moreover, Dhruv et al. (2002) demonstrated that the application of electrical noise at the feet improved the detection of Semmes-Weinstein filaments among a cohort of older individuals, and successful detection increased with increasing noise amplitude (20-80% of sensory threshold).

A logical extension from the evidence that non-zero noise (often 90% of sensory threshold) improves stimuli detection at the feet is to examine a task in which tactile information detected with the feet is important for successful completion. Thus examining how enhancing tactile sensation impacts the control of standing posture, an activity reported to be important to quality of life among those with sensory loss (Cattaneo et al., 2002). A number of studies have examined how SR can enhance postural control (Costa et al., 2007; Magalhaes & Kohn, 2011a; Priplata et al., 2002; Reeves, Cholewicki, Lee, & Mysliwiec, 2009). These studies form the foundation for understanding how SR can enhance postural control in those with clinically impaired sensory loss. Priplata et al. (2002) examined the effects of white-type mechanical noise application to the soles of the feet (90% perception threshold) and found that adding noise reduced postural sway in young and older participants. The older group's postural sway was changed such that the application of SR resulted in values similar to those that naturally occur in the younger cohort. As both young and older participants exhibited

similar reductions in sway, suggesting that age is not a determining factor in the efficacy of noise enhanced postural control through SR-type behavior (Priplata et al., 2002).

Electrical noise, applied simultaneously to the triceps surae and tibialis anterior, has been reported to improve postural sway (displacement, peak velocity and area) when this noise is applied at a level that minimizes force variability of the muscles spanning the ankle joint (85, 90 or 95% of sensory threshold) (Magalhaes & Kohn, 2011a). Significant correlations were found between reductions in force variability and postural sway parameters (sway area and RMS of postural COP position in the anterior-posterior direction) (Magalhaes & Kohn, 2011a). These findings led the authors to conclude that setting a noise level such that it minimizes torque variability at the ankle would elicit the best postural improvements (Magalhaes & Kohn, 2011a). Additionally Costa et al. (2007) reported that the application of SR to the soles of the feet improved the complexity of the postural COP pattern. The application of SR to the soles of the also reduced sway parameters during quiet standing among a variety of populations including young (Priplata et al., 2002), the elderly ((Costa et al., 2007; Priplata et al., 2003; Priplata et al., 2006), those with diabetic neuropathy (Priplata et al., 2006), and stroke patients (Priplata et al., 2006). Still others have demonstrated that subthreshold noise improves balance when applied to light touch situations (Kimura et al., 2012; Magalhaes & Kohn, 2011b) and for those suffering from low back pain (Reeves et al., 2009).

The use of tactile noise has shown great promise as a way to enhance postural control in a wide range of populations. The current availability of small mechanical stimulation devices allows for SR based aids to provide improvements in postural control across a wide range of clinical and aging populations in real-world settings. Further

research is necessary to determine whether noise-based sensory enhancements improve balance in postures other than quiet stance, such as forward and rearward leaning. These postures push the postural COP toward the borders of the feet (Cavanaugh et al., 1999), and having access to the maximum amount of sensory information may allow for improved stability in these challenging postures. It is also necessary to gain further understanding of whether it is possible to use standard clinical sensory tests (e.g., filament and biothesiometer) to set the noise level that best elicits postural improvement. Additional investigation is also needed to examine how adjusting noise parameters in different parts of the foot could change how the foot is used (i.e. pressure patterns) during standing and walking. Demonstrating that enhancing stimulus detection with the foot, through SR behavior, can lead to altered planter pressure patterns would indicate a strong link between perception and action at the foot.

2.6.5 Summary of Techniques for Enhancing Posture

Resistance and balance training, biofeedback, vibration and stochastic resonance have all displayed different degrees of improvement measures of postural control. However, none have identified a definitive mechanism by which postural stability is improved. A wearable aid that applies SR signals to the feet appears to be a method that can robustly improve postural control in a variety of populations, through the enhancement of cutaneous sensation. Thus, through SR enhanced sensation, there is the ability to improve the underlying causes of postural instability, opposed to other techniques that aim to improve compensatory responses.

CHAPTER III

PROPOSED METHODS

3.1 Participant Characteristics

The studies of this dissertation aim to expand the understanding of how cutaneous sensory function impacts the control and perception of posture. To facilitate this we will recruit female participants between 18-40 years of age with no known deficits in visual, vestibular, muscular, or somatosensory function. The rationale for choosing this population is that 1) women are reported to exhibit a greater loss in sensation for a given decrease in skin temperature compared to men (Liou et al., 1999), and 2) selecting young healthy individuals will limit the possible effects of age on sensory function (Illing et al., 2010). Additionally, examining this population allows for the elimination of comorbidities found in clinical populations that may influence postural control (e.g., neural degeneration, cognitive deficits and vestibular impairment). Restricting the sample to healthy participants allows for the assumption that any observed changes in the control and perception of posture can be attributed to the experimental conditions. These choices will therefore allow for Studies 2 and 3 to assess the loss of sensation in a controlled manner.

The number of participants necessary for each study was identified using results from pilot work and the current literature. Sample size estimations were obtained for all three studies using $\alpha=0.05$ and $\beta=0.80$ in accordance with traditional practice (Table 3.1). Pilot work examining the differences in the magnitude of minimum detectable stimulus between supine and standing postures was used to estimate a minimum sample size of

seven for Study 1. Sample size estimates for Study 2 were calculated from the absolute repositioning error data obtained from Fujiwara et al. (2003) for the recreation of postures that place the COP location at 40, 50, and 60% of foot length. Estimates took into account data from the aforementioned postures both with and without participants' feet being cooled. The resultant power analysis indicates a minimum sample size of 11 is necessary to see temperature-mediated changes in the ability to reposition posture. A sample size estimate of 11 was calculated for study 3 based on data available in Costa et al. (2007); specifically, we utilized Costa et al.'s data examining differences in the COP complexity in young and older individuals due to application of SR signals to the soles of the feet. For all three studies I propose a sample size of 12 participants, as these values are similar to or greater than those estimated.

Table 3.1 Sample Size Estimations. Criteria for sample size calculations α =0.05 and β 0.80

Study	Variable	P-value	Sample Size Estimate	N	Citation
1	% Change in Minimum Detectible Stimulus (Standing vs. Supine)	n/a	7	3 - Female	Pilot Work
2	Difference in cooled vs. uncooled feet for repositioning error 40-60% of foot length	40% - p<0.01 50% - p<0.05 60% - p< 0.01	11	8 – Male 8 - Female	Fujiwara et al. 2003
3	% in Complexity of COP position with application of SR signals.	ML – 0.02 AP – 0.03	11	15 – young 12- elderly	Costa et al. 2007

3.2 General Procedures and Equipment

Upon arrival to the University of Massachusetts Motor Control Laboratory, all participants will provide written informed consent to procedures approved by the University of Massachusetts Amherst Institutional Review Board. At this time a verbal introduction will be given to the participant, explaining the procedures for the relevant study or studies in which they are participating. Participants will be instructed to abstain from caffeine for three-hours prior to arriving at the laboratory. Upon completion of the informed consent and introduction, participants will change into clothing appropriate for data collection, e.g., shorts and tank top. Anthropometric measures (e.g., height, weight and foot length) will be collected, after which subjects will perform a series of psychophysical and postural tasks, outlined below.

Two types of measurement devices will be used during psychophysical experiments. Participants will be asked to identify vibrating cutaneous stimuli for the assessment of sensory ability in supine, quiet standing and forward leaning postures. Stimuli will be presented using a biothesiometer, a clinical tool commonly used for the assessment of the minimal detectable stimulus. All biothesiometer measurements will be taken with footwear off. The biothesiometer will be used to assess the voltage of the minimum detectable stimulus bilaterally at the heel and the 3rd metatarsal head, fore- and rearfoot, respectively, for the supine posture only. As the biothesiometer does not allow for stimuli to be presented in non-supine postures, additional measurements will be made using C-2 tactors embedded in a pair of customized Teva sandals (Deckers Outdoor Corporation, Goleta, CA) (Figure 3.1). Tactors will be used to assess sensory function at the same locations as the biothesiometer, and will be applied at all three postures. Supine

measures from the biothesiometer and C-2 tactors will subsequently be compared; a strong correlation between the two devices will confirm whether the tactors produce clinically relevant measurements in those postures where only the tactors can be applied.

Figure 3.1: Custom Sandals with C-2 Tactors

In the first experiment postural assessments will be made on a 50 cm x 50 cm RSscan mat (RSscan International, Belgium). The second and third experiments will use a 120 cm x 60 cm force platform (Advanced Mechanical Technology Incorporated (AMTI), Watertown, MA) for the assessment of COP dynamics. Kinematic data will be collected using a three-dimensional motion capture system (Qualysis, Gothenburg, Sweden). The postural data collection space will be calibrated such that the corner of the platform will serve as the origin of the Laboratory Global Coordinate System and the Local Coordinate System of the force platform; all data will be collected in the first

spherical quadrant. Kinematic data will be collected via passive, low-density, infrared markers (Figure 3.2).

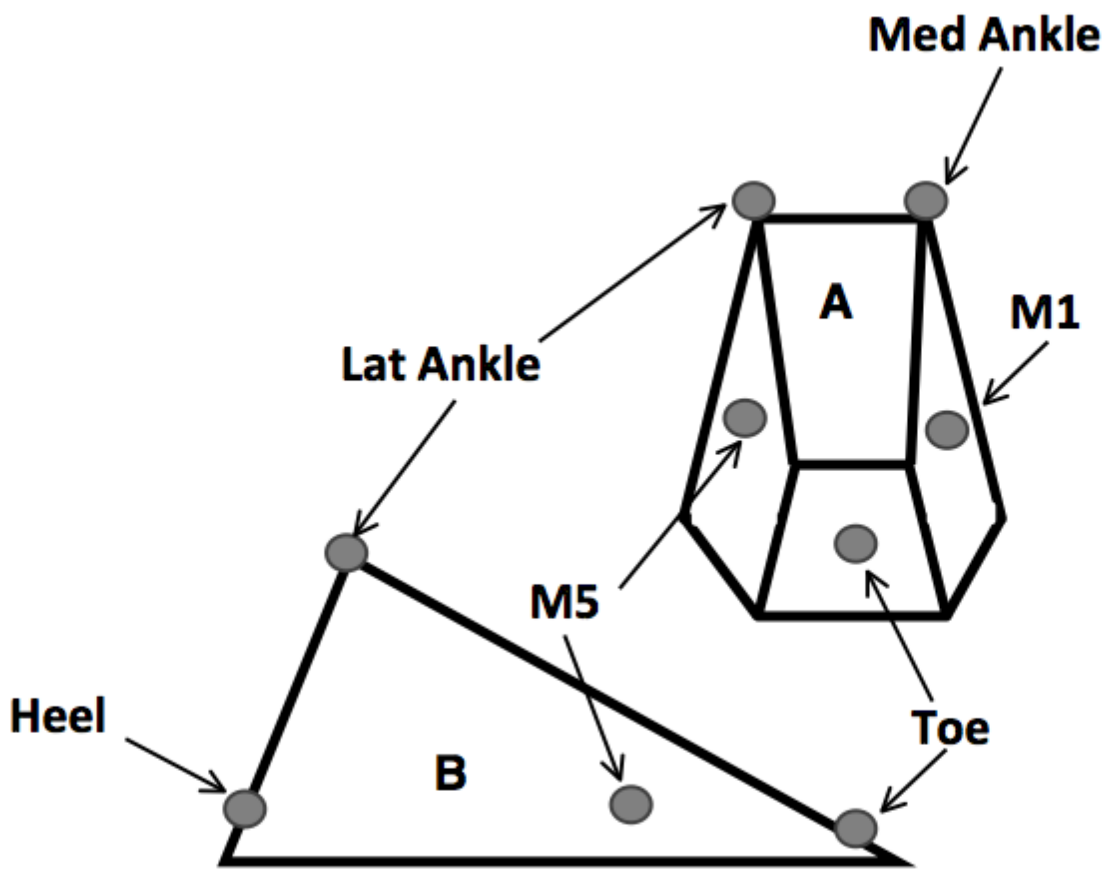

Figure 3.2: Placement of Foot Markers: Circles represent markers placed on anatomical landmarks of the foot. A) Frontal and B) Saggital View

Prior to participants' arrival, the data collection area will be calibrated in accordance with Qualysis data collection procedures (standard deviation of the calibration wand distance should be less than 1.0 mm). A single step in the anterior-posterior and medial-lateral directions will be used to visually inspect that the resultant ground reaction force vector has the proper orientations for the x, y and z forces prior to

testing. The force platform will be zeroed prior to each trial. The force plate and lab coordinate systems will be configured such that the positive-x direction is in the anterior direction, positive-y direction points to the subject's left and the positive-z direction is pointing upward from the force plate.

Post processing for the kinematic and kinetic data will be done in Qualysis Track Manager (QTM) software, and exported to text files (.txt) for further analysis using custom MATLab (Mathworks, Natick, MA) and C++ programs. Calibration trials will be saved for each study to ensure that relationships between markers are precisely recorded.

3.2.1 Description of Tactor Shoes

Teva sandals will be customized such that they place C-2 tactors at the heel and 3rd metatarsal head (Figure 3.1). The tactors are mounted such that only a small (0.3" diameter) probe will contact the subject's foot. The use of this footwear allows for the measurement of sensory function while in standing postures.

Vibrations sent to the tactors will be modulated by a laptop running TactorSDK 2.1 software with noise plug-in. This laptop will be connected to an AEI ATC-3 controller via a Bluetooth connection (Engineering Acoustics, Inc., Cassellberry, FL). The controller allows for one or multiple tactors to be simultaneously activated with a constant white noise profile of 30-350 Hz; signal amplitude is further modulated by adjusting voltage.

3.3 Study 1: The Effect of Posture on Plantar Surface Cutaneous Sensation

The aim of this study is to gain an understanding of how pressure changes under the foot influence the ability to detect cutaneous stimuli. To investigate this, the plantar pressure and the minimum detectable stimulus will be assessed in three postures: supine, quiet upright standing, and forward lean. These three postures were selected in order to assess how the ability to identify external stimuli changes when different pressures occur under each portion of the foot.

3.3.1 Study 1 Procedures

During each of the three postures the minimum detectable stimulus and the pressure will be assessed bilaterally at the center of the heel (rearfoot) and the head of the 3rd metatarsal (forefoot). The minimum detectable stimulus will be assessed with both a biothesiometer and C-2 tactors in the supine position, while only the C-2 tactors will be used to assess the minimum detectable stimulus during quiet upright standing and forward lean postures. The amplitude of the biothesiometer stimulus will be increased gradually until each participant is able to identify that the probe is vibrating. Participants' minimum detectible stimulus will be identified with the C-2 tactors via a modified 4-2-1 method. Subjects will be presented with ascending stimuli (weak-to-strong) with a reversal from ascending to descending stimuli at first identification and another at each non-identification/identification point, until a voltage is assessed at which identification is made at one voltage and non-identification is made in triplicate at the next lowest voltage (Chong & Cros, 2004). All sensory measures will be made in duplicate as is

standard procedure, and the order of stimulus locations will be randomized between trials.

While participants are in the quiet standing and forward lean postures, we will also assess the pressures under the forefoot and rearfoot. During each of the trials, 5s of plantar pressure data will be collected from an RSscan mat. This information, collected at 100 Hz, will be used to identify the average pressure under the same regions of the feet at which minimum detectable stimulus was assessed.

Participants will be given instructions for each posture. In the quiet standing posture, participants will be instructed to stand in a relaxed manner such that they do not lift any part of the foot from the floor and do not weight one foot more than the other. They will be given a demonstration and will have adequate practice to ensure they are standing in an appropriate manner. In the forward lean posture participants will be instructed to shift their body weight to the balls of their feet by rotating about the ankle and maintain the posture such that they do not lift their heels from the floor. The supine position will be assessed when participants lie on their back on an examination table. Participants will wear noise-canceling headphones during all postures so that they will not be able to hear the audible buzz of the tactors. This choice is made so that participants identify the location of the stimulus only through the cutaneous sensory structures of the foot. Examination of the dependent variables from this study will provide information as to how changing the pressure under the feet influences the ability to detect external stimuli.

3.3.2 Study 1: Dependent Variables

The minimum detectable stimulus will be collected by two different methods; the biothesiometer and the C-2 tactors. In the case of the biothesiometer the voltage (V) of the minimal detectable stimulus will be recorded, and the average of two trials at each foot location will be calculated. The tactors will be used to assess the voltage of the minimum detectible stimulus (mV); the average of two trials at each foot location will be calculated.

The plantar pressure under each foot will be collected during each of the sensory trials via the RSscan Mat, and the pressures under the forefoot and the heel will be averaged over the middle 3s of the 5s data recording to generate a representative pressure in each portion of the foot. This procedure will be repeated for all trials where participants perform standing postures, as described in section 3.3.1. The supine position will have a zero value for pressure, as no weight-bearing pressure is applied to the feet. We do acknowledge that some pressure from the sandals on the foot is likely in this position; however this pressure is minimal and not fundamentally different in nature to that of holding the biothesiometer to the foot.

3.3.3 Study 1: Statistical Evaluation of the Hypotheses

Each of the individual hypotheses will be statistically evaluated using the dependent variables described above. All analysis of variance (ANOVA) and regression measures for this study will be evaluated for significance at $\alpha=0.05$. Prior to evaluation of the hypotheses, pairwise t-tests will be used to compare pressure and sensory data between the right and left feet of each participant. If no significant differences are

detected between the two feet, the variables will be averaged to form representative values. If significant differences are detected, the data from each foot will be kept separate. Additionally, the pressures under each portion of the foot will be compared via pairwise t-test to ensure that changing posture from quiet standing to forward lean fundamentally changes the pressure under the fore- and rearfoot, as expected.

Hypothesis 1a anticipates that the three postures: supine, quiet standing, and forward lean will exhibit differences in the minimum detectable stimulus in both the fore- and rearfoot locations. This hypothesis will be evaluated using a one-way repeated measures analysis of variance (RM-ANOVA). The independent, repeated measures will be posture (supine, quiet upright standing and forward lean) and foot location (fore- and rearfoot of each foot), while the dependent measure will be the average magnitude of the minimum detectable stimulus at each foot location for each participant.

Hypothesis 1b anticipates a significant positive relationship between the pressure under the feet and the magnitude of the minimum detectible stimulus. We will model the data by fitting first, second and third order linear regressions, with the magnitude of the minimum detectible stimulus treated as the dependent variable in all models. All foot locations and postures will be included in one regression analysis. The hypothesis will be supported if the effect of the pressure under the feet on the minimum detectible stimulus is significant in each model. R^2 values will be used to compare the three candidate models and make a recommendation as to which model best fits the data, with the maximum r^2 denoting the best model.

Hypothesis 1c-e, (Table 3.1) will be examined using the data from study 1a. Following the RM-ANOVA (described above), a least square differences post-hoc

analyses will be conducted to examine the pairwise relationships between pressure, posture, and foot location. The anticipated pattern for the minimum detectable stimulus of the forefoot and rearfoot is identified in Table 3.1.

Table 3.2 Anticipated Relationships for the Minimum Detectible Stimulus of Fore- and Rearfoot

Foot Location	
Forefoot	Forward Lean > Quiet Upright Standing > Supine Position
Rearfoot	Quiet Standing > Forward Lean > Supine Position

Hypothesis 1c will be supported if the magnitude of the minimum detectable stimulus in the rearfoot is greatest in quiet standing, as compared to the supine and forward lean postures. Additionally, the magnitude of the minimum stimulus required in the forefoot in quiet standing will be greater than in the supine position but less than in the forward lean.

Hypothesis 1d will be supported if the pairwise comparisons in both the fore- and rearfoot demonstrate the minimum detectible stimulus will be lowest in the supine position compared to quiet upright standing and forward lean.

Hypothesis 1e will be supported if the magnitude for detection in the forefoot is greatest in forward lean, as compared to both supine and quiet standing postures. The magnitude of the minimum stimulus required in the rearfoot in forward lean will be greater than in the supine position, but lower than in the quiet standing posture.

Hypothesis 1f will be supported if a Pearson-product moment correlations reveal strong positive relationship between the biothesiometer and C-2 tactor measurements in the supine position, in both the fore- and rearfoot.

3.4 Study 2: The Effect of Impaired Sensory Function on the Control of Upright Posture

The aim of this study is to enhance our understanding of how the ability to identify external cutaneous stimuli influences the perception of body orientation and control of the postural COP. The ability to detect sensory stimuli will be systematically impaired through a controlled reduction in skin temperature (Weitz, 1941). It is anticipated that each reduction in skin temperature will confer a decrease in postural performance. If this relationship is observed it will provide evidence supporting the hypothesis that decreases in cutaneous sensory ability directly affect the control of posture. This relationship is expected as clinical populations that exhibit an increase in the magnitude of the minimum detectable stimulus exhibit concurrent losses in the control of posture (Van Emmerik et al., 2010) and perception of the COP position (Fujiwara et al., 2003).

3.4.1 Study 2: Procedures

In this study participants will undergo a series of successive skin temperature reductions. After each reduction they will be asked to repeat a series of postural assessments. Two types of data will be collected and analyzed: psychophysical and kinetic.

The skin temperature on the plantar surface of the foot will be reduced in a stepwise manner by placing the feet on a plate cooled by ice water. Participants' feet will be placed on the cooling plate until the skin temperature is reduced by 4, 8, and 12-degrees Celsius (ST-4, ST-8 and ST-12, respectively) from the baseline skin temperature. The baseline skin temperature is defined as the point at which a less than one degree

change in the participants skin temperature is observed over a ten minute time span, allowing for participants feet to adjust to the ambient room temperature. Skin temperature will be monitored via an infrared thermometer (Exergen Corp., Watertown, MA). Once each of the four skin temperatures is achieved, participants will undergo psychophysical (2a) and postural (2b and 2c) assessments. During experimentation participants will spend no more than 120s without having their feet on the cooling plate, to ensure that skin temperature does not increase significantly (Nurse & Nigg, 2001).

The psychophysical portion of this study (hypothesis 2a) will involve using the custom built Teva sandals to stimulate the feet at the four different skin temperature conditions. These temperatures have been reported to significantly elevate the magnitude of minimum detectable stimulus (Weitz, 1941). In each temperature condition, the voltage of the minimum detectable stimulus will be recorded in both supine and quiet standing postures at the same locations on the foot as in study 1 (bilateral heel and 3rd metatarsal head).

The perception of body orientation (hypothesis 2b) will be assessed through a postural repositioning task. Participants will be given verbal feedback to guide them through a series of anterior leans that displace the postural COP through ankle joint rotation. These postures displace the COP to a distance of 50% and 60% of the foot length forward from the most posterior portion of the foot. These distances were selected as they have previously been reported to elicit the greatest changes in the ability to reposition the body when cutaneous sensation was impaired (Figure 2.4) (Fujiwara et al., 2003). A device will be placed between the participants' feet such that the net COP position can be positioned within a window that corresponds to 5% of foot length (Figure

3.3). The center of this window will be placed at 50% and 60% of the foot length, measured from the most posterior portion of the foot. Once participants correctly position

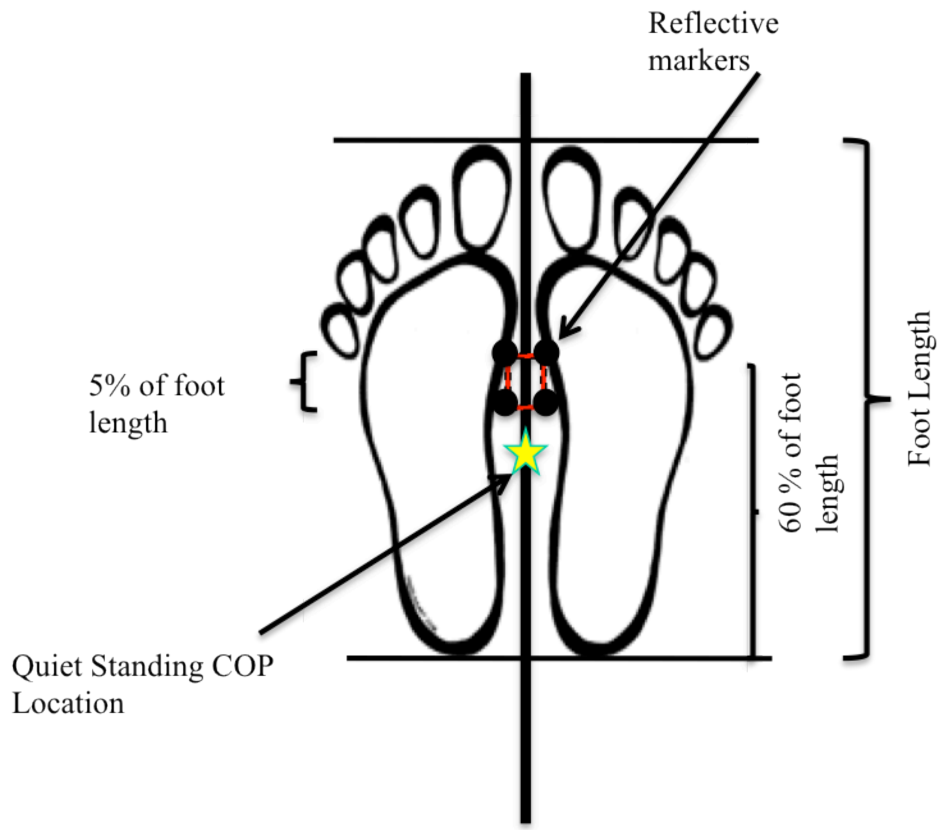

Figure 3.3: Apparatus for Postural Repositioning. Demonstrates how the window (5% of foot length) is placed so that the center of it is at 50 & 60% of the length of the foot. (*not to scale)

their COP, they will be instructed to hold each of these reference positions for 5 seconds while the forces and moments are measured by the force platform (AMTI, Watertown, MA). These forces and moments will be used to calculate the COP position. Participants will then be seated for at least 5 seconds prior to being instructed to recreate the reference posture. This will ensure that subjects have to fully recreate the posture. Once they feel that they have best repositioned themselves they will verbally notify the examiner, and

the kinetic information necessary for COP calculation will again be recorded for 5 seconds. During both the reference positioning as well as the repositioning participants will have their vision occluded, via an opaque eye mask.

Hypothesis 2c, which evaluates how cooling the feet impact the control of the postural COP, will be assessed during quiet standing in each of the four temperature conditions in a progressive manner from warmest to coldest (ST-0, ST-4, ST-8 and ST-12). During this task, participants will be instructed to stand in a relaxed manner such that they do not lift any part of the foot from the floor and such that they do not weight one foot more than the other. They will be given a demonstration as to what quiet standing is, and will have adequate practice to ensure they are standing in an appropriate manner. This posture will be held for 40 seconds, while forces and moments are collected. Again these forces and moments will be used to calculate the net COP position. During this postural task, vision will be occluded via an opaque eye mask.

3.4.2 Study 2: Dependent Variables

The minimum detectable stimulus will be collected by two different methods; the biothesiometer (supine position only) and the C-2 tactors. In the case of the biothesiometer the voltage (V) of the minimal detectable stimulus will be recorded and the average of 2 trials at each foot location will be calculated. The minimum detectable stimulus (mV) will be assessed with the C-2 tactors in the supine and quiet upright standing postures. For each posture, the average of the two trials will be calculated in all foot locations and used as the minimum detectable stimulus. In each trial, the actual temperature of the skin (degrees Celsius) at each treatment level will be recorded. As

with the sensory measures, the temperature measurements from the two trials will be averaged.

The minimum detectible stimuli for all four foot sites will be added together to create a minimum detectible stimulus score for each temperature condition. This composite measure will allow for comparison of how net sensory function impacts the perception of body orientation and control of the postural COP.

The postural COP position will be calculated using the force and moment data collected by the force platform (Eqn. 3.1). Prior to processing, COP position data will be smoothed using a 4th order Butterworth lowpass filter with a 4 Hz cutoff for the postural repositioning (2b) and bandpass filtered 1-20 Hz for the complexity analysis (2c) (Mathworks, Natick, MA).

Kinematic data will be used to derive postural time-to-contact and center of mass measures and will be used in secondary analysis (i.e. not directly associated with the hypotheses outlined in this dissertation).

The absolute positioning error will be used to evaluate the performance in the postural repositioning task. The reference position is the x,y coordinates of the COP position relative to a virtual point that represents the middle of the two ankle joints, in the transverse (x,y) plane, during the 3-second positioning task. The COP position is calculated from the forces and moment collected from the force plates (Eqn 3.1, Figure 3.5)

$$COP_x = (-M_y + F_x z) * F_z^{-1}$$

$$COP_y = (M_x + F_y z) * F_z^{-1} \qquad \text{Eqn 3.1}$$

where x and y are the resultant coordinates of the COP location, M_x and M_y are the moments about the x or y-axis, F_x and F_y are the forces in the x or y-axis and z is the distance of the load cell from the force platform surface. This measurement will be transformed such that the COP measurement, described in Eqn. 3.1, will transformed such that it lies in the global coordinate system, allowing for both kinematic and kinetic measurements to be in coincident coordinate systems. This allows the COP position to be measured relative to a virtual point between the ankles, rather than relative to a point on the platform, thereby negating any effect of the participant moving between trials. The reproduced position will be the 3s average of the x,y position of the COP position during each of the two repositioning trials. The positioning error will be calculated as the absolute linear difference between the reference position and the reproduced position (Eqn. 3.2).

$$repositioning\ error = \frac{\sqrt{\left(\bar{x}_{rep} - \bar{x}_{ref}\right)^2 + \left(\bar{y}_{rep} - \bar{y}_{ref}\right)^2}}{foot\ length} \qquad \text{Eqn. 3.2}$$

where $\bar{x},\bar{y}_{\mathrm{rep}}$ and $\bar{x},\bar{y}_{\mathrm{ref}}$ are the three second average of the x and y positions in the reproduced and reference positions, respectively.

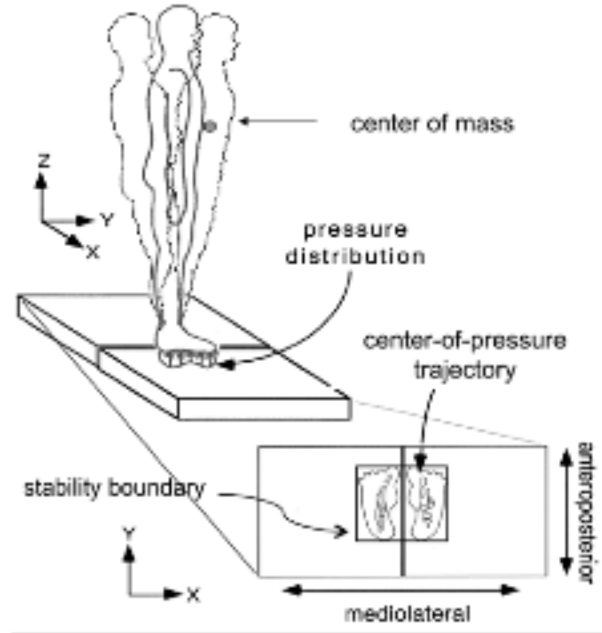

Figure 3.4: Platform Posturography. Depiction of postural COP excursions in anterior-posterior and medio-lateral directions. Also indicated are the whole body center-of-mass and the stability boundary, formed by the borders of the feet. (Van Emmerik et al., 2013)

3.4.2.1 Multiscale Entropy

The complexity of the postural COP time series will be calculated using the MSE procedure. The MSE calculation is made up of a three-step process:

1) A coarse-grained time series will be constructed by dividing the original time series into non-overlapping windows, dictated by the scale factor τ_m (Eqn. 3.3):

$$y_j^{\tau} = \left(\frac{1}{\tau}\right) \sum_{i=(j-1)\tau+1}^{j\tau} x_i, 1 \leq j \leq N/\tau \qquad \text{Eqn. 3.3}$$

Where x_i is the time series data points and N is the time series length. This study will examine scale factors 1 through 15, corresponding to 33.33-2.2 Hz fluctuations.

2) The sample entropy (S_E) will then be calculated (Eqn. 3.4):

$$S_E(m,r,N) = -\ln\frac{U_{(m+1)}(r)}{U_m(r)} \qquad \text{Eqn. 3.4}$$

Where *U* is the probability that two points, within a window of comparison, *m,* are within the radius of similarity, *r*. The radius of similarity will be determined, for each sample, as 15% of the standard deviation of the original COP time series. This value has been consistently used in the literature for the evaluation of biological signals (Costa et al., 2005; Costa et al., 2007). The window of comparison, *m,* was selected as 2, as this allows for the greatest number of comparisons. This analysis compares the likelihood that a point m points apart is similar to that of length m+1. S_E will be analyzed for both the AP and ML directions.

3) The complexity index, C_i, will be calculated by taking the area under the MSE curve (Eqn. 3.5), generated by plotting the S_E and scale factor on the ordinate and abscissa, respectively.

$$C_i = \sum_{i=1}^{N} S_E(i) \qquad \text{Eqn. 3.5}$$

3.4.3 Study 2: Statistical Evaluation of the Hypotheses

All analysis of variance and regression measures for this study will have significance at α=0.05. The three individual hypotheses of this study, outlined in section 1.8.2.3, will be evaluated independently.

Hypothesis 2a anticipates that lowering the temperature of the feet will increase the magnitude of the minimum detectable stimulus. This will be evaluated using a one-way repeated measures analysis of variance (RM-ANOVA) with the magnitude of the stimulus applied to the feet by the tactors as the dependent variable and the different

temperature conditions (ST-0, ST-4, ST-8 and ST-12) as the independent-repeated measure. If main effects are observed for temperature, a least squares difference posthoc analysis will be used for pairwise temperature comparisons. Additionally, the exploratory hypothesis will be supported if the RM-ANOVA model exhibit a significant negative relationship for a first, second or third order regression model. R^2 values will be used to compare the three candidate models and make a recommendation as to which model best fits the data, with the maximum r^2 denoting the best model.

If the predicted curvilinear relationship exits, the minimum detectible stimulus will be log converted based on the order of fit. This will linearize the sensory data and allow for a comparison between the repositioning and complexity data in the subsequent hypotheses.

Hypothesis 2b predicts that decreases in foot temperature will impair the ability of participants to accurately recreate each reference posture, measured as an increase in the positioning error. To test this hypothesis, a RM-ANOVA will be used to examine how the dependent measure of positioning error changes during the different temperature conditions. If main effects for temperature are observed, a least squares difference posthoc analysis will be used to make pairwise temperature comparisons. Additionally, the exploratory hypothesis will be supported if first, second or third order curve fits of the RM-ANOVA model exhibit a significant positive relationship. R^2 values will be used to compare the three candidate models and make a recommendation as to which model best fits the data, with the maximum r^2 denoting the best model.

Hypothesis 2c predicts that a decrease in foot temperature will elicit a decrease in complexity of the postural COP pattern. To test this hypothesis, a RM-ANOVA will be

used to examine the dependent measure of the complexity index at each repeated temperature condition (ST-0, ST-4, ST-8 and ST-12). If a main effect for temperature is observed, a least squares difference posthoc analysis will be used to make pairwise temperature comparisons. Additionally, the exploratory hypothesis will be supported if first, second or third order curve fits of the RM-ANOVA model exhibit a significant positive relationship. R^2 values will be used to compare the three candidate models and make a recommendation as to which model best fits the data, with the maximum r^2 denoting the best model.

3.5 Study 3: The Effect of Stochastic Resonance on Postural Control in the Presence of Cutaneous Sensory Loss

The aim of the third study is to gain understanding as to how stochastic resonance (SR) affects the control and perception of the postural COP in the presence of a reduced ability to identify cutaneous sensory stimuli. It has been previously demonstrated that SR can enhance the identification of cutaneous sensory stimuli; that is, stimuli that were previously not identifiable become distinguishable when SR is applied (Collins et al., 1996b). Additionally, it has been reported that SR can improve postural control in populations that exhibit reduced sensory function (Priplata et al., 2003; Priplata et al., 2002; Priplata et al., 2006). It is not clear, however, whether it is the improved detection of cutaneous stimuli that mediates the improvement in postural control. To this end, this experiment will seek to examine whether or not SR can improve the control of the postural COP and perception of body position in otherwise healthy individuals when the ability to identify cutaneous stimuli is reduced.

3.5.1 Study 3: Procedures

Study 3 will use procedures similar to those in Studies 2b and 2c to determine if application of SR to the sole of the foot can improve the perception and control of posture. Ideally, this study will use the same participants as Study 2. Cold plates will again be implemented to reduce the temperature of plantar surface of the feet. Studies 3a and 3b will evaluate the perception of body position and control of the postural COP under three skin temperature conditions: 1) the normally occurring skin temperature (ST-0); 2) the skin temperature from study 2a which has the biothesiometer measurements most characteristic of individuals with mild-to-moderate multiple sclerosis (Remelius et al., 2012), a population which exhibits both balance and sensory deficits; and 3) the skin temperature that exhibited the greatest increase in the voltage of the minimum detectable stimuli in study 2a, as assessed by the biothesiometer in the supine position.

In this study, SR signals will be applied to the feet using a single-blind design, such that the presence of SR signal is unknown to the participant. The SR signal magnitude will be set to 90% of the minimum detectable stimulus of the most sensitive foot location, and this is consistent with the current literature (Collins et al., 2003; Priplata et al., 2003; Priplata et al., 2002; Priplata et al., 2006). This signal level has previously been identified as the signal intensity that demonstrated the greatest improvement in postural control among clinical populations (Collins et al., 2003; Priplata et al., 2003; Priplata et al., 2002; Priplata et al., 2006).

The perception of body position (3a) will be assessed through a postural repositioning task. The repositioning task will follow the same procedures as Study 2b, with the modification that SR signals will be applied to the plantar surface of the feet in

50% of the trials. Trials will be randomized and SR signals will be of a magnitude that is undetectable to participants. Participants will complete two trials with and two without SR signals applied to their feet, for a total of four postural repositioning trials per lean and temperature condition. When participants feel they have reoriented to the reference position they will notify the researcher and 5s of kinetic information (forces and moments) will be collected from the force platform and used to calculate the postural COP position. As in Study 2b, participants will have their vision occluded via an opaque eye mask during both the reference positioning as well as the repositioning task.

The control of the postural COP (3b) will be assessed during quiet standing in each of the three temperature conditions outlined above. The procedures for this task will be the same as in Study 2c. During this task participants will be instructed to stand in a relaxed manner such that they do not lift any part of the foot from the floor and do not weight one foot more than the other. They will be given a demonstration as to what quiet standing is, and will have adequate practice to ensure they are standing in an appropriate manner. This posture will be held for 40 seconds, while forces and moments are collected. As with study 3a, four trials will be collected, two with and two without SR signals applied to the sole of the feet. Again, these forces and moments will be used to calculate the net COP position. The complexity of the postural COP time series will be compared between trials where SR signal is present and those where it is absent. As in Study 2c, participants will have their vision occluded via an opaque eye mask.

3.5.2 Study 3: Dependent Variables

The dependent variables used to evaluate the hypotheses in Study 3 are the repositioning error and the complexity index of the postural COP time series. The details for the construction of the repositioning error and complexity index are described in section 3.3.2. In addition to these variables, it will be noted for each trial whether or not the SR signal was applied.

3.5.3 Study 3 Statistical Evaluation of the Hypotheses

All measures in Study 3 will use $\alpha=0.05$ to identify significant differences between temperature and SR conditions. Pearson-product moment correlations will be assessed as strong relationships at $r > |0.8|$. All three of the individual hypotheses of this study, outlined in section 1.8.3.3, will be evaluated independently.

Hypothesis 3a predicts that the application of SR signals to the feet will improve the ability to reposition the body to the reference when cutaneous sensation is impaired through cooling. A two-way repeated measures analysis of variance (RM-ANOVA-2) will be used to evaluate the effect of temperature and the presence of SR signals on the ability to accurately reposition the postural COP position. For this analysis the dependent variable will be the error in postural repositioning and the repeated independent variables will be foot temperature condition (ST-4, ST-8, and ST-12) and the presence of SR signal.

Hypothesis 3b predicts that the application of SR signals to the feet would increase the complexity of the postural COP when sensation is impaired through cooling. A RM-ANOVA-2 will be used to evaluate the effect of temperature and the presence of

SR on the complexity index of the COP time series. For this analysis the dependent (within-subject) variable will be the COP complexity and the repeated independent variables will be the three temperature conditions and the presence of SR signal.

Hypothesis 3c predicts that the application of SR signals will increase the complexity of the postural COP time series in a baseline-dependent manner. That is, the level of improvement achieved in the complexity of the COP signal through the application of SR is expected to be greater with increased levels of sensory impairment (and increasing cooling of the skin). This hypothesis will be supported if there is a significant negative relationship between the skin temperature of the foot and the difference in the complexity index between trials where SR was applied and those where SR was not applied.

3.6 Potential Methodological Problems

All indications are that cooling the feet will effectively reduce the ability to identify external stimuli and that the manner in which this happens will be equal across all receptor types (Billot et al., 2013; Lowrey et al., 2013). However, there exists the possibility that, even with the occlusion of vision and a reduced ability to identify external stimuli, no differences will be observed in the measures of perception and control of the postural COP. A pilot test examining the effect of the specific temperatures selected will take place prior to execution of studies 2 and 3. The exact temperatures the feet are cooled to will be dependent on pilot work, were the final temperature selection will be based on selecting temperatures that elicit changes in cutaneous sensation.

In spite of these potential problems, the choices made in this set of studies are supported by the current literature. There exists the possibility that differences between the experimental conditions will not be severe enough to impair the postural function of healthy, young participants. Even if this is the case, these studies still provide knowledge that healthy systems are able to adapt to maintain adequate control over the postural COP and body orientation in the presence of impaired sensory function.

Additionally, the choice of primary dependent measures that examine only the spatial aspects of the COP control may prove inadequate for the identification of differences between experimental conditions. To overcome these potential issues, there exists the possibility to calculate the MSE of the COP velocity as well as to utilize boundary relevant measures, e.g., postural time-to-contact and MSE of the postural time-to-contact. All indications are that this step should not be necessary as MSE has been shown to be more sensitive in systematically identifying differences between clinical and sub-clinical pathologies than more traditional postural measures, e.g., sway area, COP path length, COP velocity, and the minimum time-to-contact (Gruber et al., 2011). Nonetheless, with these potential alternative dependent measures, there remain several different methods for exploring how cooling of the feet influences the perception and control of the postural COP.

The third potential methodological issue that may arise is that, due to small sample sizes, the differences between experimental conditions may be incorrectly identified as non-significant by the statistical models outlined in the earlier portions of this chapter, though the conservative sample size selections made for these studies should alleviate this. However, if these models do not identify significant differences between

experimental conditions, there exists the possibility to use the methods outlined by Cohen (Cohen, 1988, 1992) that use a statistic called "effect size", where the effect of a condition is assessed by its biological impact. An effect size of 0.2-0.3 is deemed to have low-effect, 0.5 a moderate-effect and an effect size of greater than 0.8 is a large-effect. The use of this type of statistical analysis can be done on all of the dependent measures in all three studies, whereby the mean and standard deviations of each dependent variable can be used to calculate the effect size between any combination of experimental conditions.

The final potential methodological issue comes from subject compliance to the verbal instructions. This can pose problems in any study where participants are given verbal instructions, but these issues will be mitigated as much as possible in the current group of studies. Specifically, several of the tasks in the 2nd and 3rd studies involve a degree of feedback from the experimenter during the postural repositioning portion of the task. Also, during the postural control portions of studies 2 and 3, participants will be given a demonstration as to what quiet standing is and provided with subject-relevant context in which to frame the task. The issue of accurate identification of the external stimuli, which provides critical pieces of information for all three studies, will be verbally explained to the participants. In addition, participants will be given several practice sessions in which they are presented with the vibrating stimuli at a magnitude that is clearly identifiable; this will be done in all of the experimental postures to ensure that participants are familiar with the type of stimulus they are expected to identify.

CHAPTER IV

MODIFICATIONS TO PROPOSED EXPERIMENTS

4.1 Changes to Study 1

A change from the RSscan mat to two AMTI force platforms was necessary, as it became apparent that use of the RSscan mats would not be feasible as they were no longer available. Because of this, some modifications were necessary. The aim of this study was to examine how changing posture, from sitting to standing, impacts 1) the loading of the fore- and rearfoot and 2) the cutaneous sensory thresholds at corresponding locations. We originally intended to do this by examining plantar pressure. However, to pursue this aim using the AMTI force platforms, it was necessary to instead examine how changes in the magnitude of the vertical ground reaction forces that accompany shifts from sitting to standing impact the sensory thresholds under the fore- and rearfoot.

Data collection was modified such that participants identified the cutaneous stimuli under each portion of their feet while sitting or standing with the fore- and rearfoot each located on separate force platforms (Figure 4.1). Vertical ground reaction forces were captured for 5 s during the same time period that sensory thresholds were determined. No changes were made to the proposed methods for identifying the sensory thresholds.

Additionally, changes were made to the postural tasks used to assess the force/threshold relationship. This was necessary as the magnitude of stimulus required at the forefoot during forward leans was often larger than could be generated by the tactor control unit. To circumvent this issue, a seated posture was substituted for the forward

lean. This change maintained the aims of the study, whereby we were able to assess changes in sensory threshold due to the different plantar loadings that accompany shifts in posture.

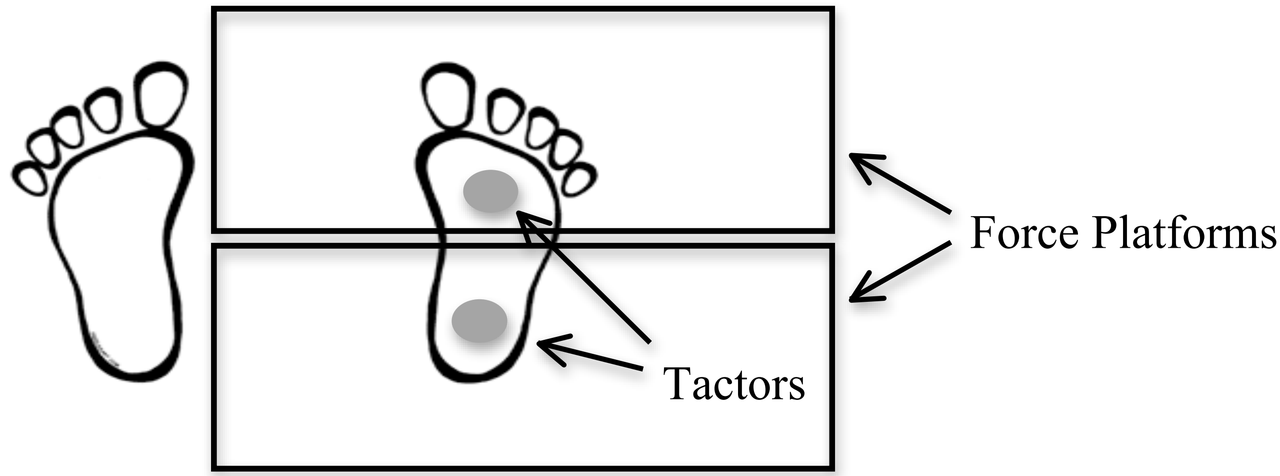

Figure 4.1: Configuration for Assessing Foot Sensation. Used in both the seated and quiet standing postures (Right Foot), not to scale.

Changes were also made to the data analysis procedures. In order to understand the relationship between cutaneous sensory function and the forces under the foot, we ran the same analysis as originally proposed for the pressures, only force was used as the dependent variable *in lieu* of pressure. An additional change was that linear mixed model analysis of variance (ANOVA) were used instead of repeated measures ANOVA, as it allows all subjects to be included in the analysis even in the case of missing data due to a corrupt trial. Using a linear mixed model ANOVA also allowed for similar statistical methods to be used across all analyses and maintain continuity through the entire dissertation. Additionally, the fixed factor for foot was classified in two ways: 1) left/right and 2) the amount of weight borne (more/less). This change acknowledges that postural asymmetries may not arise in a manner that can be identified by separating the feet solely based on left/right differences. Rather, separating the feet based on the

amount of weight they bear may better identify how different postures, as well as asymmetries in those postures, impact the ability to detect external stimuli. The linear mixed model ANOVA will be used in place of the proposed regressions, as the postures in this study do not cover a sufficient range of foot loading for regressions to be informative.

4.2 Changes to Study 2

Instead of having data collections, as originally proposed, the data for the second and third studies were collected at the same time. This change afforded the best control of the environmental conditions (temperature, humidity) in the lab. This proved to be important, as the conditions in the UMass biomechanics laboratory were quite variable.

In study 2, participants underwent only one trial (as opposed to the proposed two trials) of each of the postural tasks: repositioning and quiet standing. This choice was made in response to the finding, during pilot work, that temperature reductions of the feet could only be maintained for 120 s before warming appreciably (Appendix E). As the neural response to cyclical warming and cooling of the skin remains unknown, participants only performed one postural repositioning and one quiet standing trial at each temperature condition, thus allowing the tasks to be completed during the 120 s window.

Linear mixed model ANOVAs using repositioning error and MSE did not reveal significant differences in the corresponding measures of perception and control of quiet standing in response to changes in skin temperature. Therefore, detrended fluctuation analysis (DFA) was performed on the quiet standing time series. The specifics of the DFA parameters are outlined in chapters 6 and 7. The purpose for including this analysis

was to assess the level of constraint of the COP position time series. By identifying changes in the relationship between short and long time scale fluctuations in the postural COP we are able to assess the health of the systems that underlie these fluctuations. Specifically, when physiological processes that occur at short time scales contribute to those occurring at longer time scales individuals are likely to produce a system that is more robust and capable of responding to variation or disturbance.

Several other linear mixed model ANOVAs were also performed on variables created from this COP signal: mean velocity, standard deviation of velocity, MSE of the velocity time series, as well as DFA analysis of the velocity time series. Results from these analyses were not reported, as they were neither able to identify significant differences between temperature conditions nor provide additional insight as to why anticipated changes in the complexity of the quiet standing time series were not seen.

4.3 Changes to Study 3

During pilot testing it was observed that when the level of subsensory stimulation used for SR was set at 90% of the minimum detectible stimulus, some participants could periodically detect the vibrations during normal postural sway. In hindsight, this is unsurprising, as the results of the first study in this dissertation demonstrate that changing the forces under the feet impacts the ability to identify external stimuli. Because of this, we changed the SR level to 80% of the sensory threshold, a value that has also been reported to elicit improvements in the ability to detect external stimuli (Wells, Ward, Chua, & Inglis, 2005). This change is of the utmost importance as it affords an optimal level of stimulation (Figure 1.3). As the COP fluctuates across the surface of the foot, the

sensory threshold may also fluctuate; the optimal signal level is thus one that is able to enhance sensory function while remaining unnoticeable.

As in Study 2, the number of trials at each skin temperature and posture was reduced from two to one, for the same reasons outlined in section 4.2. The same changes that were undertaken for Study 2 in the quiet standing analyses were also carried out with Study 3.

4.4 References

Chong, P. S. & Cros, D. P. 2004. Technology literature review: quantitative sensory testing. *Muscle Nerve,* 29**,** 734-47.

Wells, C., Ward, L. M., Chua, R. & Inglis, T. J. 2005. Touch noise increases vibrotactile sensitivity in old and young. *Psychological Science,* 16**,** 313-20.

CHAPTER V

FORCES UNDER THE FEET IMPACT THE ABILITY TO DETECT EXTERNAL INFORMATION

Abstract:

Cutaneous sensory function is known to play a vital role in the control of upright standing, with clinical sensory loss being related to increased rates of falls as well as altered postural center of pressure dynamics. The purpose of this study was to assess how changes in forces under the feet that accompany changes in posture impact the ability to detect vibrations with the plantar surface of the foot. To accomplish this, sensory testing was conducted on 12 healthy females aged 21-40 yrs. Cutaneous sensory thresholds, defined as the smallest amplitude vibrations participants could accurately identify, were determined in three postures: supine, seated, and standing. The forces under fore- and rearfoot were assessed during sitting and standing. Results showed that sensory thresholds were significantly elevated in standing compared with both supine ($p=0.013$ and 0.002, in the fore- and rearfoot, respectively) and seated postures ($p=0.015$ and 0.002, in the fore- and rearfoot, respectively); a trend for difference between seated and supine postures was observed in the forefoot ($p=0.08$). This change in sensory ability coincided with significantly larger forces (both absolute and body weight-scaled) under both the fore- and rearfoot in standing compared with sitting ($p<0.001$; ~30% vs. ~8% body weight at each measurement site). Additionally, sensory thresholds were significantly lower in the forefoot compared with the rearfoot ($p<0.001$). Force asymmetries did not appear to alter the ability to identify external vibration between the

feet, indicating that small bilateral differences in weighting of feet are not sufficient to alter sensory thresholds. These result demonstrate that changing postures, and their corresponding changes in pressure distribution under the feet, alter the sensory thresholds such that postures that place ~8% more weight on the forefeet serve to increase the sensory threshold.

5.1 Introduction

The successful control of upright standing is influenced by multiple sensory modalities, including vision, vestibular function and cutaneous sensation (Creath, Kiemel, Horak, & Jeka, 2008; Jeka et al., 2000; Polastri et al., 2012). To date, sensory function in the foot has only been assessed in a supine posture, which places no weight on the plantar surface of the foot (Inglis et al., 2002; Kennedy & Inglis, 2002). Thus, the influence of postural tasks on the ability to detect external information at the foot-ground interface is largely unknown. Inglis et al. suggest that sensory function assessed in the supine position may not be representative of sensory function in other postures. The clinical relevance of this limitation is underscored by the work of Nurse and Nigg (2001), who reported reduced plantar pressure under sensory impaired portions of the foot during walking, compared with pressure under the same portions of the foot when sensation was not impaired. This finding suggests that plantar pressures may be modulated, such that force is shifted away from sensory impaired portions of the feet in order to improve access to external information (Turvey, 1996). These findings indicate that cutaneous sensation measured in the supine position may fail to reflect how sensory function impacts postural control and *vice versa* (Inglis et al., 2002; Patel et al., 2009), and that decreasing pressure under the foot may serve as a way to increase the detection of external information.

To elucidate the relationship between the forces imposed by functional postures on the plantar surface of the feet and cutaneous sensory thresholds, we employed a novel device consisting of C-2 tactors (Engineering Acoustics Inc., FL) embedded in the fore- and rearfoot of a pair of sandals (Figure 3.1, Teva, Deckers Outdoor Corp.,

Goleta, CA). These devices provide advantages over traditional sensory assessment techniques (e.g., Semmes-Weinstein filaments, tuning forks, and Biothesiometers) in that they can be used to quantify sensory thresholds during both weighted and unweighted postures. Traditional devices require the foot to be off the ground, thus negating the possibility of assessing cutaneous sensation in upright standing. C-2 tactors have previously been implemented to supply cutaneous stimulation to the plantar surface of the feet (Cloutier et al., 2009; Galica et al., 2009; Stephen et al., 2012), torso (Wall, 2010; Wall et al., 2009), and wrist (Tino et al., 2011) during walking and upright standing; however, these studies did not report results related to the assessment of sensory function.

The use of tactors will allow for further insights into the interactions between postures that load the feet differently and cutaneous sensory thresholds. This is important, as individuals with clinical sensory loss, assessed in non weight bearing (supine or prone) postures, display altered center-of-pressure (COP) dynamics (Bonnet et al., 2009; Cameron, Horak, Herndon, & Bourdette, 2008; Van Emmerik et al., 2013; Van Emmerik et al., 2010). Studies that improve our knowledge of how cutaneous sensory thresholds are altered during weight bearing postures will dramatically enhance our ability to contextualize the changes in COP parameters seen in groups with impaired sensory function. This is of particular relevance as impairments in postural control have been reported to pose major barriers in accomplishing activities of daily living which, in turn, severely impact quality of life (Heesen et al., 2008).

It remains unclear if the changes in COP dynamics observed among individuals with cutaneous sensory loss serve as part of a strategy to mitigate sensory dysfunction.

Van Emmerik et al. (2010) reported that a cohort of individuals with multiple sclerosis, exhibiting cutaneous sensory impairment, had greater asymmetries in the vertical ground reaction forces during quiet standing than individuals without MS, suggesting that shifts in the weighting of the feet may alter access to external information and/or body orientation. Additionally, the dense distribution of sensory receptors under the fore- and rearfoot (Kennedy & Inglis, 2002) suggests that altering the weighting of the feet, fore and aft, may enhance the ability to detect information regarding body orientation and movement. Research in direct perception suggests that individuals are able to modulate forces in meaningful ways in order to identify fundamental properties of external objects (Turvey, 1996); this ability has been demonstrated in upright standing through COP modulation (Palatinus et al., 2012).

The purpose of this study was to determine how changes in posture impact: 1) the forces applied to the plantar surfaces of the feet, and 2) the thresholds for detecting vibrations. We hypothesized that, as the forces under the feet change due to fundamental shifts in posture, e.g., moving from sitting to standing, there would be corresponding changes in the sensory threshold. This was tested by comparing the cutaneous sensory thresholds under the fore- and rearfoot of both the left and right feet during three postures: supine, seated, and quiet standing. We expected the lowest cutaneous sensory thresholds in the supine position, and the highest thresholds in standing. Additionally, we examined if individuals asymmetrically load their feet and if this impacts the ability to detect vibrations. Specifically, we hypothesized that during weight bearing postures individuals would exhibit an asymmetry in the loading of the feet, identified as a significant difference in the amount of weight borne by each foot.

Further, we hypothesized that asymmetries in the amount of weight borne by each foot would correspond to an asymmetry in the ability to detect external vibrations, identified as an increase in the cutaneous sensory thresholds under the foot that bears more weight.

5.2 Methods

5.2.1 Participants

Twelve female participants (*31.4 (4.7)* yrs, *1.65 (0.06)* m, *61.9 (7.5)* kg; mean (one standard deviation)) were recruited from the University of Massachusetts Amherst and surrounding communities. Participants provided written informed consent prior to study participation. The University of Massachusetts Amherst Institutional Review Board approved all procedures. All participants reported being free from cutaneous sensory impairment, injury, neural degeneration, cognitive deficits and visual impairments.

5.2.2 Experimental Procedures

Participants wore comfortable athletic clothes and were fitted with custom modified sandals that had C-2 tactors embedded in the sole at the center of the heel and third metatarsal head. This device was used to assess sensory thresholds, defined as the lowest voltage that individuals were able to detect, in supine, seated, and standing postures. The tactors were modulated via a modified 4:2:1 method (Chong & Cros, 2004) of sensory stimulus identification. In the 4:2:1 method for determining sensory threshold, the 30-350 Hz (white noise) signal amplitude was increased from the lowest

level four levels at a time until the participant was able to detect it. The signal was then decreased two levels at a time until the participant was unable to detect it. Finally, the signal was modulated one level at a time until neighboring vibrations produced responses where one was identifiable and the other was not.

In both the seated and standing postures, subjects placed one foot such that it spanned two adjacent AMTI force plates (AMTI, Watertown, MA), with the forefoot on one plate and rearfoot on the other plate (approximately 50% of the foot on each plate; Figure 4.1). In the seated postural condition, participants sat with their hip, knee and ankle joints at approximately 90-degree angles. During upright standing postures, participants were instructed to stand quietly, with arms at their sides. In both weight-bearing postures, kinetic data were collected for 5 s during the period during the time period that participants underwent sensory testing. During all sensory procedures participants donned noise-canceling headphones to mute the soft, audible buzz emitted by the tactors. Procedures were repeated for both left and right feet.

5.2.3 Dependent Variables

The dependent variables for this experiment were the sensory thresholds (mV), and the magnitude of the vertical ground reaction forces under both the fore- and rearfeet in absolute (N) and body weight scaled (% body weight) units. Exploring both absolute and body weight normalized forces is important as the absolute force under the feet is directly related to a participant's weight. Additionally, if individual tuning occurs at the level of the sensory receptors in response to loading, it is more likely to be done as a function of percent body weight than as a function of absolute force.

The magnitude of the vertical ground reaction forces was recorded in Qualysis Track Manager (Qualysis, Gothenburg, Sweden) from two adjacent AMTI force platforms (AMTI, Watertown, MA) at 100 Hz. Data were low-pass filtered at 4 Hz with a 4^{th} order, dual-pass, zero-lag, Butterworth filter, via custom written Matlab software (Mathworks, Natick, USA); cutoff frequency (2.5-3.5 Hz) was based on Fourier analysis.

5.2.4 Statistical Analysis

One-way linear mixed model analyses of variance (ANOVA) were used to assess main and interaction effects, with posture (supine, seated and standing), foot (left and right), and foot location (fore- and rearfoot) as fixed effects, subject as the random effect, and sensory threshold and body weighting (absolute and percent body weight, only in seated and standing postures) as the dependent measures.

Additional ANOVA models were used to assess if separating the feet by the percent body weight they bear produces asymmetries in force and sensation. This analysis was performed on only the seated and standing postures, as there was no measurable force under the feet in the supine position. Furthermore, separating the feet in a functional manner allows us to better elucidate the force/sensation relationship that may be masked by between-subject differences when separating the feet by left/right. Main and interaction effects were assessed with posture (seated, standing), foot (more/less loaded) and foot location (fore- and rearfoot) as fixed effects, subject as random effect, and sensory threshold and the forces under the feet (N and percent body weight) as the dependent measures. When main effects were found, pairwise t-tests

were used to identify the nature of these differences. All statistical procedures were performed in PASW Statistics (SPSS, v.18, Chicago, Ill). Significance is defined at $\alpha=0.05$ for all statistical tests; p-values between 0.05 and 0.10 are defined here as demonstrating a statistical trend.

5.3 Results

5.3.1 The Effect of Posture on Sensory Function and Force

The ANOVA examining changes in sensory threshold due to changes in posture revealed no interaction effects between foot (left/right), foot location (fore-/rearfoot), or posture (supine, sitting, and standing); however, significant main effects were observed for foot location and postural condition on sensory thresholds (Table 5.1, Fig. 5.1). Quiet standing exhibited significantly higher sensory thresholds compared with both the seated and supine postures, in both the fore- and rearfoot (Table 5.2). A trend for difference was observed between the sensory thresholds in supine and seated in the forefoot ($p=0.08$), however, no significant difference was observed in the rearfoot ($p=0.80$, Table 5.2). Compared with the forefoot, the rearfoot exhibited significantly elevated sensory thresholds in supine and sitting, but not in standing (Table 5.3). The seated posture exhibited significantly lower forces (both absolute and body weight-scaled) than quiet standing under both the fore- and rearfoot locations (Table 5.1).

Table 5.1: Sensory Threshold and Load Data by Posture, Foot and Foot Location

	Sensation		Force (N)		Force (%Body Weight)	
	F	p-value	F	p-value	F	p-value
Posture	16.992	<0.001*	466.63	<0.001*	727.887	<0.001*
Foot	0.430	0.513	0.017	0.898	0.12	0.730
Location	13.734	<0.001*	35.104	<0.001*	53.987	<0.001*
Posture * Foot	0.102	0.903	0.027	0.869	0.004	0.951
Posture * Location	0.070	0.933	7.002	0.010*	10.474	0.002*
Foot * Location	0.290	0.591	9.192	0.003*	15.105	<0.001*

*p<0.05, # 0.05< p < 0.10

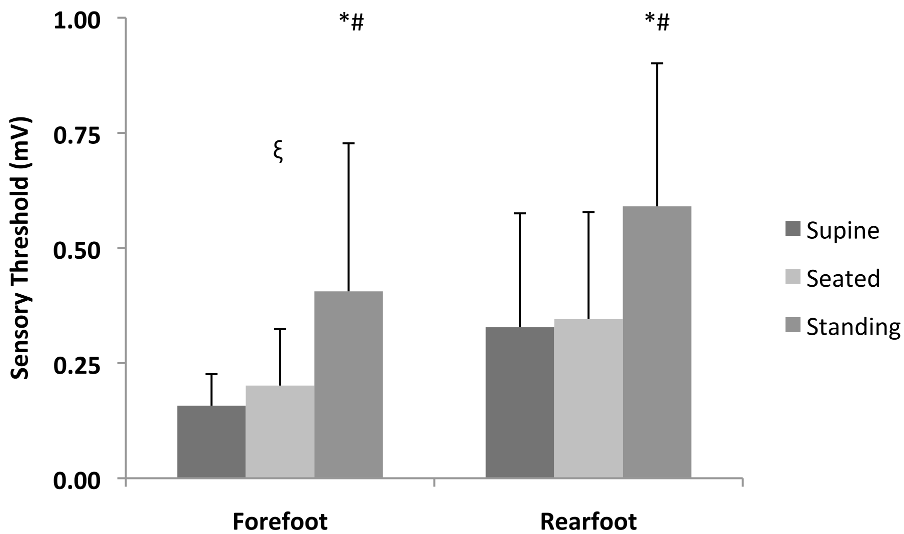

Figure 5.1: Sensory Thresholds. Values of the right and left feet are averaged, as ANOVA revealed no differences between the feet. * Significantly different than the supine posture, # significantly different than the seated posture, and ξ trend for difference from the supine posture. Statistical significance identified as p<0.05, trend identified as 0.05<p<0.10, bars represent mean + SD.

Table 5.2: Effect of Posture on Sensory Thresholds.
Results of pairwise t-tests. p-values.

		Supine	Seated
Forefoot	**Seated**	0.08#	
	Standing	0.013*	0.015*
Rearfoot	**Seated**	0.80	
	Standing	0.002*	0.002*

*p<0.05, # 0.05< p < 0.10

Table 5.3: Differences between the Fore- and Rearfoot.
Mean (SD) and p-values from pairwise t-tests.

	Forefoot Mean(std)	Rearfoot Mean(std)	p-value
Supine	0.16 (0.07)	0.33 (.25)	0.03*
Seated	0.20 (0.12)	0.35 (0.24)	0.02*
Standing	0.41 (0.32)	0.59 (0.31)	0.11

*p<0.05

5.3.2 The Impact of Loading Asymmetry on Cutaneous Sensory Function

We further separated the feet by the amount of weight they bore, less vs. more loaded. When the feet were separated in this manner, we observed significant asymmetry in the amount of weight placed on the feet (foot effect Table 5.4); this was true of both absolute and body weight-scaled measures. Additionally, we observed interaction effects for foot location-by-posture and posture-by-foot, as well as main effects of foot location, foot and posture in both measures of force (Table 5.4, Figure 5.2). These differences in forces were robust, in that all pairwise t-tests between foot, foot locations and postures revealed significant differences (Table 5.5)

Table 5.4: Asymmetry of Load and Sensory Threshold by Posture, Foot and Foot Location: Main and interaction effects for sensation and the weight borne by each foot during seated and standing postures.

	Sensation		Force (N)		Force (%Body Weight)	
	F	**P-value**	**F**	**P-value**	**F**	**P-value**
Posture	16.824	<0.001*	498.081	<0.001*	3.136	<0.001*
Foot	0.142	0.707	14.863	<0.001*	45.845	<0.001*
Location	5.311	0.024*	7.474	.008*	618.112	0.001*
Posture* Foot	0.272	0.603	4.819	0.031*	1.87	0.005*
Posture*Location	0.398	0.53	37.47	<0.001*	0.955	<0.001*
Foot*Location	0.539	0.465	0.047	0.828	8.895	0.679

*p<0.05, # 0.05 < p < 0.10

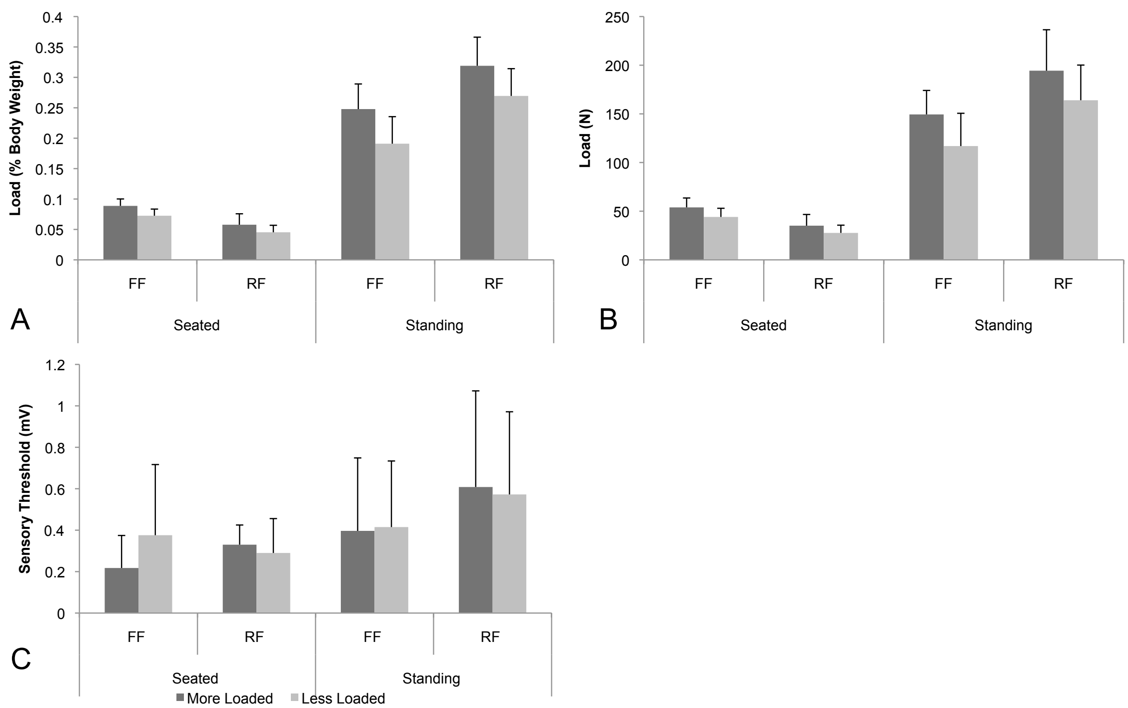

Figure 5.2: Changes in Sensation Based on Foot Loading: Forces A) Body weight scaled, B) Unscaled, and C) Cutaneous sensory thresholds under the fore- and rearfoot (FF and RF) in sitting and standing. Main and interaction effects reported in (Table 5.4), individual differences reported in (Table 5.5). Bars represent mean + SD.

Table 5.5: Post-hoc Analysis for Asymmetries: Differences between A) Feet, B) Foot Location, and C) Posture.

A		More Loaded vs. Less Loaded		
		Sensation	**Force (N)**	**Force (%BW)**
Seated	**Forefoot**	0.096#	0.001*	0.001*
	Rearfoot	0.169	0.005*	0.005*
Standing	**Forefoot**	0.798	0.006*	0.007*
	Rearfoot	0.751	0.001*	<0.001*

B		Fore- vs. Rearfoot		
		Sensation	**Force (N)**	**Force (%BW)**
Seated	**More Loaded**	0.781	<0.001*	<0.001*
	Less Loaded	0.048*	<0.001*	<0.001*
Standing	**More Loaded**	0.193	0.013*	0.011*
	Less Loaded	0.193	0.002*	0.002*

C		Seated vs. Standing		
		Sensation	**Force (N)**	**Force (%BW)**
Forefoot	**More Loaded**	0.011*	<0.001*	<0.001*
	Less Loaded	0.114	<0.001*	<0.001*
Rearfoot	**More Loaded**	0.082#	<0.001*	<0.001*
	Less Loaded	0.003*	<0.001*	<0.001*

*p>0.05, # 0.05<p<0.10

The assessment of sensory function under the more and less loaded feet revealed significant main effects for foot location and posture (Table 5.4; p=0.024 and p<0.001, respectively). A significant difference was observed between the sensory thresholds of the fore- and rearfoot in the less loaded foot in the seated posture (Table 5.5; p=0.048), where the forefoot exhibited elevated sensory thresholds. There was a trend for difference between the more and less loaded feet in the forefoot during the seated posture (p=0.096), where the less loaded foot exhibited elevated sensory thresholds compared with the more loaded foot.

5.4 Discussion

The purpose of this study was to determine how differences in the magnitudes of the forces on the plantar surface of the feet, which are associated with changes in posture, impact the ability to detect vibrations with the foot. Shifting from sitting to standing, and the accompanying large change in forces under the feet (from ~8 to ~30% body weight borne at each measurement site, Table 5.1), significantly increases the sensory thresholds in both the fore- and rearfoot (50-100% increase in stimulus magnitude, Figure 5.1). Furthermore, it appears that even the subtle change in the weighting of the feet (from ~0 to ~8% body weight) that accompanies a shift from lying supine to sitting may be enough to elevate sensory thresholds in the forefoot. These results suggest that both the fore- and rearfoot respond to increases in weight, but the forefoot appears to be more sensitive to these changes than the rearfoot. Interaction effects likely result from between-subject differences in the weighting of the feet and the nature of different postures, wherein standing individuals place 100% of their weight on their feet, while during sitting only 25% of the body weight is borne by the feet.

Additionally, participants asymmetrically loaded the feet in both sitting and standing (Table 5.4), which agreed with our hypothesis. However, contrary to our hypothesis, we did not observe significant differences in the sensory thresholds between the more and less loaded feet. While the magnitude of difference between the feet was significant, the small magnitude (Figure 5.2a, ~1% and ~5% differences in force between the more and less loaded feet at both the fore- and rearfoot in sitting and standing, respectively) appears to be too small to elicit changes in the sensory

thresholds. This result is consistent with what was seen when the feet were separated anatomically (left/right). Large increases in the amount of weight borne by the feet (sitting to standing) were sufficient to increase the sensory thresholds, but the small differences in the amount of weight borne between the more and less loaded foot (~5%) were not enough to alter the sensory thresholds between the feet. Therefore, it appears that while healthy individuals asymmetrically load the feet, they do so in a manner that does not elicit changes in cutaneous sensory thresholds. Larger magnitudes of loading asymmetry between the feet may serve as a way to mitigate the effects of sensory loss, as clinical populations have been shown to have a larger asymmetry in loading (~16% of body weight) than what was observed with this cohort of young healthy women (Chung et al., 2008).

Examining the sensation of both the fore- and rearfoot appears to be important as the forefoot consistently exhibits lower sensory thresholds than the rearfoot. This may come about by the increased concentration of fast acting mechanoreceptors in the forefoot, compared with the rearfoot, and provides evidence that the forefoot may be better suited to advantageously adapt to postural asymmetries than the rearfoot (Kennedy & Inglis, 2002). In general, postures placing greater force on the plantar surface of the feet impair the ability to detect external vibration, and the asymmetrical loading of the feet among healthy individuals is not sufficient to elicit differences in the ability to detect external vibration (Figure 5.2, Table 5.3).

This experiment expands our knowledge by demonstrating that the forces applied to the plantar surface of the foot impact the ability to detect environmental information. Heretofore, research has been limited to examining: the distribution of the

sensory receptors on the foot (Kennedy & Inglis, 2002), the roles these receptors play in the control of posture (Inglis et al., 2002), and how altering sensory function impacts plantar pressure fluctuations during gait (Hohne, Stark, & Bruggemann, 2009; Nurse & Nigg, 2001). Though much is already known about the distribution of the sensory organs that populate the plantar surface of the feet (Wells et al., 2003) and their role in identifying vibratory stimuli of different frequencies (Kennedy & Inglis, 2002), it remains unknown how individuals modulate the pressure under their feet in a way that provides access to environmental information. Additionally, it is unclear if the differences in postural sway patterns between clinical and non-clinical populations emerge as a strategy to increase the ability to identify vibrations, as imposed in this experiment, or other types of external or exproprioceptive information (i.e., relating one's body position to the environment).

It appears that a postural strategy that reduces the force/pressure under sensory impaired portions of the foot may have the ability to improve the ability to detect vibrations. Evidence that postures which place lower forces on the plantar surface of the feet also exhibit lower sensory thresholds (Figure 5.2) supports the suggestion that reducing force under the feet may be a means to improve the detection of external vibrations. Furthermore, the results of Nurse and Nigg (2001) appear to be congruent with this strategy, where reductions in cutaneous sensation, brought about by a cooling of the feet, elicited shifts in plantar pressure away from sensory impaired portions of the feet during walking.

Hohne et al. (2009), on the other hand, did not observe shifts in the COP when sensory function was removed from the entire plantar surface of the foot via an

anesthetic solution. This is not necessarily surprising, as changing the pressure under a specific area of the foot would confer no sensory advantage when the entire plantar surface was anesthetized. We show here that postures tat place less force on the sole of the foot exhibit lower sensory thresholds. In combination with the work of Nurse and Nigg, these results suggest that the alteration of COP patterns among individuals with clinical sensory loss may be a strategy for improving the ability to identify environmental information, though the way in which this occurs remains unclear.

Given that COP fluctuations can be modulated in a way that allows for the direct perception of environmental information (Palatinus et al., 2012; Turvey, 1996), our results suggest that it is likely individuals have the ability to modulate the forces under their feet in a manner that tunes cutaneous sensation to the task at hand. Future experiments should focus on elucidating how changes in COP fluctuations, observed in clinical populations, alter the ability to identify cutaneous information. Such research will afford greater insight into the manner by which active movement can facilitate the detection of external information, thereby providing further context in identifying whether or not the altered COP patterns observed among individuals with clinically based sensory loss are adaptive or maladaptive. This, in turn, would allow us to further evaluate postural fluctuations in a manner in accordance with J.J. Gibson's eloquent statement, "We move to perceive and perceive to move" (Gibson, 1962).

The results of this study support Gibson's statement by demonstrating that actively altering the force under the plantar surface of the feet (movement) appears to change the ability to detect external vibrations (perception). However, while the results of this work provide evidence that movement and perception are linked, they do not

identify the manner in which humans modulate postural pressure patterns in order to maximize sensory function. The changes in sensory thresholds brought about by moving from sitting to standing suggest that increasing the pressure on the plantar surface of the feet impairs the ability to detect external vibration. That is, modulating the pressure under the feet in a manner that reduces pressure concentrations may allow individuals with sensory loss to partially mitigate the effects of altered sensory status. Currently, it appears that subtle changes in amount of weight borne by the forefoot are sufficient to elicit changes in the ability to detect external vibrations, while a greater amount of force change was needed in the rearfoot.

5.5 Conclusion

The findings of this study indicate that increased force on the plantar surface of the feet leads to significant reductions in the ability to detect external vibration. Specifically, small changes (<10% of body weight) elicited trends for a change in sensation in the forefoot, though larger differences (amount unknown) are needed to confer changes in the rearfoot. Furthermore, individuals appear to weight their feet in an asymmetrical manner, although among healthy individuals the small differences between the feet (~5% of body weight) are insufficient to elicit changes in the ability to detect external information. The observed changes in sensory threshold in response to the amount of weight borne by the feet, explored here in young healthy women, provides a foundation for assessing the role that altering plantar pressure may have on ability to detect external vibrations among individuals with clinically based sensory loss.

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CHAPTER VI

IMPAIRED SENSORY FUNCTION IMPACTS THE CONTROL AND PERCEPTION OF UPRIGHT POSTURE

Abstract:

Cutaneous sensory loss is thought to contribute to the impairments in balance observed in many clinical disorders. However, examining how cutaneous sensory loss impacts upright standing among individuals with clinical disorders is difficult, as comorbidities often influence control and perception of upright standing. We therefore aimed to assess how cooling the plantar surface of the foot, a manipulation that impairs cutaneous sensation, impacts cutaneous sensory thresholds, and if these changes affect the perception and control of upright standing. Twelve healthy females (21-40 yrs) underwent sensory and postural testing at four skin temperatures (baseline, 5, 9 and 14°C below baseline) with vision occluded. Vision was occluded in order to place maximal reliance on cutaneous sensory information. We evaluated how reducing skin temperature impacted: cutaneous sensory thresholds, ability to reposition the body, and the complexity (multiscale entropy) and long-range correlations (detrended fluctuation analysis (DFA)) in postural center of pressure fluctuations. Progressively cooling the feet elevated sensory thresholds, such that each decrease in skin temperature further impaired sensation. Incrementally cooling the feet increased the DFA scaling exponent of the medial-lateral postural center-of-pressure. Lowering skin temperature did not, however, impact the complexity index or ability to reposition the body. The lack of change in the complexity index may be due to the high level of constraint that appears

to be present with vision occluded. Additionally, the lack of observed change in the ability to reposition the body indicates that cooling the feet does not diminish cutaneous sensation to a level that impacts the perception of body position. The observed increase in the scaling exponent of the medial-lateral center-of-pressure that accompanies a step-wise cooling of the skin indicates that impaired cutaneous sensory feedback in the feet leads to alterations in the postural fluctuations that occur at long time scales (>250 ms). The results presented here suggest that moderately cooling the feet is an effective way to elicit clinical levels of sensory loss in otherwise healthy individuals, and allows for the assessment of how impaired cutaneous sensation impacts the control and perception of posture without the confounding factors that accompany many clinical disorders.

6.1 Introduction

Loss of cutaneous sensory function is observed in a wide range of clinical disorders, including diabetes and multiple sclerosis, as well as in aging (Cameron et al., 2008; Cavanagh et al., 1993; Citaker et al., 2011; J. K. Richardson, 2002). Reduced cutaneous sensory function has been associated with increased fall risk and changes in postural center-of-pressure (COP) parameters (Menz, Morris, & Lord, 2006; Van Emmerik et al., 2010). Jeka and colleagues have demonstrated that limiting visual, vestibular and cutaneous sources of information directly impact postural fluctuations (Creath et al., 2008; Jeka et al., 2000) and that individuals are able to dynamically reweight their reliance on a specific sensory modality based on its reliability (Oie et al., 2002; Polastri et al., 2012). For example, if visual information is compromised, increased reliance will be placed on cutaneous sensory information and vice-versa. This reweighting process likely occurs in the presence of neurodegenerative disease, as individuals try to maximize the reliability of the information they detect from the environment in the face of diminished sensory capacity. Therefore, in order to assess the direct influence of cutaneous sensory function on the control of upright standing, we need to develop methodologies that maximize the system's reliance on cutaneous sensory information, without the confounding influence of other factors that can adversely influence postural fluctuations, such as those brought on by clinical comorbidities.

Researchers have used controlled reductions of skin temperature (Fujiwara et al., 2003; Nurse & Nigg, 2001; Weitz, 1941, 1942) as well as pharmacological agents (Hohne et al., 2009) to successfully reduce cutaneous sensation. Importantly, only cooling appears to impair sensory function in a manner that mimics clinical

somatosensory loss (Lowrey et al., 2013). Others have shown that extreme cooling of the plantar surface of the skin yields systematic changes in the control (Billot et al., 2013) and perception (Fujiwara et al., 2003) of posture. These studies, however, cool the skin to a level that effectively removes cutaneous sensation (~1°C), which is not relevant for contextualizing the effect of clinical sensory loss on the perception and control of upright standing, as individuals with clinical sensory loss still maintain partial cutaneous sensory function. Furthermore, cooling the skin of women has been reported to elicit a greater degree of sensory loss than in male counterparts (Liou et al., 1999). In this study we aim to modulate skin temperature in young, healthy women in a way that elicits clinically relevant levels of cutaneous sensory loss and assess how this impacts posture.

We have previously shown that postures that place more pressure on the plantar surface of the feet increase cutaneous sensory thresholds (Chapter 5). These results support the suggestion of Inglis and colleagues, who postulated that the assessment of sensation in unweighted postures may not accurately reveal sensory ability when the tissue is loaded, such as during upright standing (Inglis et al., 2002; Kennedy & Inglis, 2002). Here, we explore how experimentally impairing cutaneous sensation impacts the perception (e.g., how well participants can recreate postures) and control of upright standing.

We evaluated the perception of postural orientation using a repositioning task. Fujiwara et al. (2003) pioneered this method and used it to demonstrate that cooling the feet to a level that severely impairs cutaneous sensation diminishes the ability to perceive body position. Additionally, this same group reported that individuals have an impaired ability to recreate postures that place the COP in the middle of the foot compared with

leans that place the COP near either the anterior or posterior border of the foot (Fujiwara et al., 2010; Fujiwara et al., 2003). They suggest that the reason for these differences is that postures that place the COP near the middle of the foot rely more heavily on cutaneous information and minimize contributions from the stretch receptors spanning the ankle. It appears that Fujiwara's temperature manipulation, which severely impaired cutaneous sensation, had the most impact on the perception of postures that relied heavily on cutaneous sensory information, but it remains unclear just how *clinical* levels of sensory loss relate to the ability to accurately perceive body position.

In addition to gaining more insight into the role of cutaneous sensation in perceiving body orientation, it is important to understand how cutaneous sensation impacts the control of upright standing. This requires the use of a different set tasks and analysis techniques than those used to assess postural perception. Multiscale entropy (MSE) and detrended fluctuation analysis (DFA) are nonlinear time series analyses that allow identification of changes in the intrinsic dynamics of the postural COP pattern during quiet standing. MSE is a measure that assesses complexity, which quantifies the nature of the interactions between the degrees of freedom that underlie more gross level behaviors in a system, where a reduction of complexity is indicative of a reduced number of functional interactions in the system. Reductions in postural complexity, identified by reductions in MSE, have been reported in older adults with clinical sensory loss, compared to those without sensory loss (Costa et al., 2007; Kang et al., 2009; Manor et al., 2010). The reduction of complexity, in general, is thought to be a function of a breakdown in either the processes that underlie physiological function (e.g. neural signaling and motor redundancy) or the interactions between these processes, which are

Furthermore, MSE has been shown to be more sensitive than other measures of COP in distinguishing between subgroups of individuals with scoliosis (Gruber et al., 2011), and appears to be well suited to identify subtle changes in the complexity of posture due to cooling the feet.

While MSE is an analysis of complexity over a range of discrete time scales, DFA assesses how the fluctuations of a time series change over a range of time scales. The scaling exponent, identified as the slope of the line fit to the log/log plot of the fluctuations versus the window length over which these fluctuations occur, allows for a quantitative assessment of how the fluctuations change over different time scales. Comparing the scaling exponent (α) from DFA analysis with signals of known structures (0.5, 1.0 and 1.5 are known for white, pink and Brownian noise, respectively) (Duarte & Sternad, 2008; Peng, Havlin, Stanley, & Goldberger, 1995) allows for the assessment of constraint in the signal. Brownian noise, which exhibits minimum complexity, is characteristic of events which occur at short time scales and have little impact on those which occur at longer time scales, whereas in pink noise, also referred to as 1/f noise, where f is the frequency of the signal, the processes that occur at short time scales contribute to those at longer time scales. Kim et al. (2008) observed a shift from pink noise type fluctuations to Brownian noise type fluctuations when vision was removed during a quiet standing task. Changes in this direction are thought to be indicative of a constrained, less adaptable, system (Duarte & Sternad, 2008). It should be noted that while the scaling exponent characterizes the fluctuations in a biological system over a range of timescales, it is not directly related to the complexity of the time series, as it does not address functional variability. Rather, the scaling exponent identifies the way in

which the postural signal repeats itself over different time scales (Lipsitz, 2002). Furthermore, this claim has been supported by the recent demonstration that mathematical models of Brownian motion are possible with the removal of the stochastic terms and indicate a high level of determinism in Brownian dynamics, which is indicative of an unadaptable or constrained system (Huerta-Cuellar, Jimenez-Lopez, Campos-Canton, & Pisarchik, 2014).

The purpose of this study was to examine the effect of cooling the plantar surface of the feet on the ability to detect external vibrations, the control of posture, and perception of body orientation. Specifically, we aimed to investigate if stepwise cooling of the feet: 1) elicited an increase in cutaneous sensory thresholds, 2) impacted perceived orientation of the body, and 3) impaired the control of posture. We hypothesized that lowering the skin temperature of the foot would: 1) increase the threshold for detecting vibrations applied to the skin, and that each subsequent decrease in skin temperature would further increase the threshold; 2) impair the ability to recreate postures, identified by an increase in the repositioning error; and 3) decrease the complexity index and increase constraint (α-values approaching 1.5) for the postural COP time series, assessed by MSE and DFA, respectively.

6.2 Methods

6.2.1 Participants

Twelve female participants were recruited from the University of Massachusetts Amherst and surrounding communities (29.4 (4.9) *yrs*, 1.65 (0.07) *m*, 57.7 (20.3) *kg*; mean (one standard deviation)). Participants provided written informed consent prior to

study participation. The Institutional Review Board at the University of Massachusetts Amherst approved all procedures. All participants reported being free from cutaneous sensory loss, injury, neural degeneration, cognitive deficits and visual impairments.

6.2.2 Experimental Procedures

The temperature of the plantar surface of the feet was allowed to stabilize to the ambient temperature of the room (less than 1°C change in 10 minutes). Sensory function was then assessed in supine and quiet standing postures by biothesiometer (Bio-Medical Instrument Co., Newbury, OH) and C-2 tactors (Engineering Acoustics, Inc., Casselberry, FL), respectively. When tactors were in use, participants wore noise-canceling headphones to mute the soft audible buzz of the device. Next, participants completed a series of postural repositioning and quiet standing tasks for the assessment of the perception and control of posture, respectively. During each of the postural tasks, participants had their vision occluded by an opaque eye mask. Vision was occluded in order to increase reliance on cutaneous sensory information. Polastri et al. (2012) suggest that a large degree of intersensory reweighting can occur; when the reliability of one modality is compromised, the reliance is shifted toward a more reliable mode. Therefore, by eliminating visual information, individuals will shift reliance on cutaneous sensation in the control of upright standing. Sensory and postural measures were repeated with the targeted skin temperatures reduced by 4, 8 and 12°C below the baseline temperature (Figure 6.1). All skin temperature measurements were made with an Exergen DX1001 infrared thermometer (Exergen Corp., Watertown, MA).

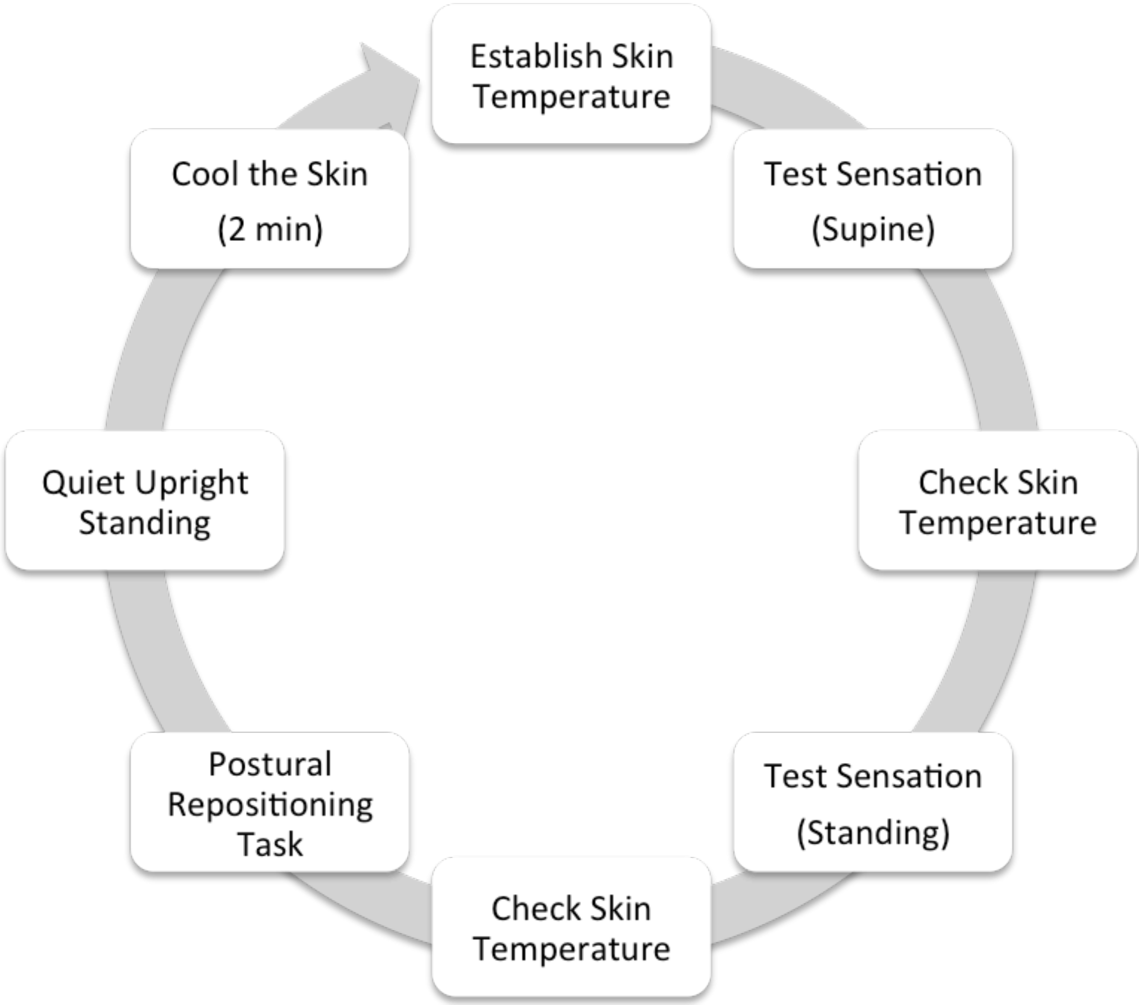

Figure 6.1 Procedures for Sensory and Postural Testing at each Skin Temperature. An illustration of the procedural order used at each skin temperature. The end of each cycle indicates a change from one temperature condition to another. At each step where the skin temperature was checked, if the skin had warmed by more than 1°C the feet were placed back on the ice until the skin temperature returned to the established temperature.

The specific skin temperature conditions were achieved by placing the plantar surface of the foot on ice for two-minute intervals. After each interval, skin temperature was reassessed; additional cooling occurred as necessary to reach target temperatures. Skin temperatures were assessed between tasks that took more than 1 minute to complete; if the feet had warmed more than 1°C, further cooling was used to return skin

temperature to the target level. The average of the temperatures taken before and after the tasks was used as a representative value for each temperature condition.

Sensory function was assessed in both supine and standing postures. In both postures, sensory thresholds were measured on the plantar surface of the left and right feet at approximately the 3rd metatarsal head and the center of the heel. In the supine posture, participants were asked to identify the onset of vibration as the oscillation (120 Hz) amplitude of the Biothesiometer probe was gradually increased. During quiet standing, sensory function was assessed by C-2 tactors embedded in the soles of custom modified sandals (Teva, Deckers Outdoor Corporation, Goleta, CA), using a 4:2:1 technique (Chong & Cros 2004). In the 4:2:1 method for determining sensory threshold, the 30-350 Hz (white noise) signal amplitude was increased from the lowest level four levels at a time until the participant was able to detect it. The signal was then decreased two levels at a time until the participant was unable to detect it. Finally, the signal was modulated one level at a time until neighboring vibrations produced responses where one was identifiable and the other was not. With both devices, sensory threshold was identified as the lowest voltage at which participants could detect the vibration.

All postural assessments were performed on one AMTI force platform (AMTI Corp., Watertown, MA), surrounded by 11 Qualysis cameras (Qualysis, Gothenberg, Sweden); kinetic and kinematic data were collected at 100 Hz in Qualysis Track Manager (Qualysis, Gothenberg, Sweden).

A postural repositioning task was used to assess the perception of posture. During this task, participants were coached into a lean that placed the COP 60% of the foot length forward of the heel through rotation about the ankles. This posture places the COP

forward of that which normally occurs in quiet standing (~45% of the foot length forward from the heel) (Fujiwara et al., 2003). This position was identified by the experimenter, who viewed the net ground reaction force in real time in the data collection software and verbally instructed participants to “lean forward, backward, left or right” until the vector passed through a target placed such that the center was between the feet, 60% of the foot length forward of the posterior border of the feet (Figure 3.3). Participants were instructed to maintain this position for 5 s while gaining perceptual awareness of their postural orientation. Participants then sat for at least 5 s prior to recreating the coached posture to the best of their abilities. This period of sitting between coached and recreated postures was included to wash out the coached posture prior to asking the participant to recreate it. Once participants felt they had recreated the coached position, they verbally notified the examiner, at which point they were instructed to maintain it for 5 s. In both the positioning and repositioning task, COP position was collected for 5 s, with the first 3 s used to assess the ability to recreate the posture. To ensure that shifts in foot position between the coached and recreated postures did not impact the measurement of repositioning error, passive markers were placed approximately at the midpoint of the posterior side of the heels; COP positions were calculated relative to the midpoint of heel markers.

The control of posture was assessed during quiet standing. Participants were instructed to stand with their feet at a comfortable width and arms at their sides. The quiet standing posture was maintained for 40 s, during which COP position was recorded.

6.2.3 Construction of Dependent Variables

6.2.3.1 Sensory Thresholds

The voltages of the sensory thresholds were used as the dependent values in statistical analysis. Values from supine and standing postures were assessed by biothesiometer and C-2 Tactors, respectively.

6.2.3.2 Postural Repositioning

Repositioning error was assessed by the differences in the COP location between the reference and reproduced leans, relative to the midpoint between the heels. This is calculated as:

$$repositioning\ error = \frac{\sqrt{\left(\bar{x}_{rep} - \bar{x}_{ref}\right)^2 + \left(\bar{y}_{rep} - \bar{y}_{ref}\right)^2}}{foot\ length} \qquad \text{Eqn. 6.1}$$

where $\bar{x},\bar{y}_{\text{rep}}$ and $\bar{x},\bar{y}_{\text{ref}}$ are the three-second averages of the x and y positions in the reproduced and reference positions, respectively. The repositioning error, as a percentage of foot length, was used as the dependent variable in statistical analysis.

6.2.3.3 Quiet Standing

The control of quiet upright standing was assessed by MSE and DFA of the anterior-posterior (AP) and medial-lateral (ML) COP position time series. The area under the sample entropy (S_E) vs. time scale curve was computed over 7 time scales, ranging from 30-210 ms. The MSE procedure consisted of calculating the S_E values (Richman & Moorman 2000) of the coarse-grained time series and numerically integrating the S_E vs. time scale curve to calculate the value of the complexity index (C_I). (For a more complete

explanation of procedures see Costa et al. (2002) and Goldberger et al. (2000) as well as section 3.4.2.1). S_E parameters were set to r = 0.15 and m = 2. C_I was used as the dependent variable in statistical analysis.

DFA was also assessed for COP position time series during quiet standing, with non-overlapping windows of sizes 4 to N/4 used to assess the linearly-detrended fluctuations, where N is the total number of samples in the time series (Peng et al., 1995). This corresponds to window sizes ranging from 40 ms – 10 s. The slope of the resulting log/log plot of *n vs. F(n)* was taken as the value of the scaling exponent (α). The scaling exponent was used as the dependent variable in statistical testing.

6.2.4 Data Reduction

When analyzing postural data, outliers were removed from the data to ensure that errant measurements did not influence the patterns assessed in DFA or MSE analysis, nor create a shift in the average position used in the repositioning error calculation. Outliers were identified as any point x, where x<25^{th} percentile-1.5*IQR or x>75^{th} percentile+1.5*IQR (where IQR is the interquartile range). Time series were then filtered with a 4^{th} order recursive Butterworth filter with cutoffs tailored to the specific analysis. A lowpass cutoff of 4 Hz was used for the (re)positioning trials; quiet standing trials were filtered with bandpass cutoffs of 2 and 20 Hz for the MSE analysis in order to eliminate drifts in the data. The time series was not filtered for DFA analysis, as high pass filtering this data has been shown to remove long-range correlations. All filtering was done via custom written MATLAB software (Mathworks, Natick, MA).

6.2.5 Statistical Analysis

The impact of decreasing the plantar surface skin temperature on sensory function during supine and standing was assessed via separate linear mixed model analyses of variance (ANOVA), with skin temperature condition (baseline, baseline-4, baseline-8 and baseline-12), foot (left/right) and location (fore- and rearfoot) as fixed factors, and the voltage of the minimum detectible stimulus (mV) from the biothesiometer and C-2 tactors as the dependent measures. If main or interaction effects were found, pairwise t-tests were used to assess where specific differences occurred. If no main or interaction effects for sensation were observed for the factors of foot (left vs. right), location (fore- vs. rearfoot) or the foot-by-location interaction, sensory values were summed to create a sensory score for post hoc analysis.

The impact of plantar surface skin temperature on the perception and control of posture was assessed by separate linear mixed model ANOVAs. In these ANOVAs the skin temperature condition was used as a fixed factor and the repositioning error, complexity index (C_I), and scaling exponent (α) as the dependent measures. Significance was assessed at $\alpha=0.05$ for all statistical tests, and trends identified as $0.05<p<0.10$.

6.3 Results

6.3.1 Impact of Cooling the Feet on Sensation

Exposing the plantar surface of the feet to ice, with the intention of lowering skin temperature 4°C at a time, actually cooled the feet on average 5.4°C, 9.1°C and 14.0°C below baseline. These reductions in temperature significantly increased sensory thresholds during both supine and standing postures (p-values<0.001; Table 6.1, Figure

6.2). No interaction effects were seen between foot, foot location and posture (Table 6.1). Additionally, post-hoc analysis showed that each subsequent decrease in skin temperature resulted in significant increases in the sensory threshold, relative to the previous temperature (Figure 6.2).

6.3.2 The Impact of Cooling the Feet on the Control and Perception of Posture

Cooling the feet significantly increased the scaling exponent (α) in the ML of the COP position time series (p=0.016, F=3.981, Figure 6.3). However, no difference was observed in the AP direction for the scaling exponent (p=0.849, F=0.266). No differences were observed in the ability to reposition the body (p= 0.669, F=0.523, Figure 6.4), or the complexity of the COP position in either the AP or ML direction (p=0.641, F=0.565 and p=0.862, F=0.249, respectively, Figure 6.5).

Table 6.1: Sensory Thresholds in Sitting and Standing Postures: Tactors used in standing. Biothesiometer used in supine. These results indicate that the temperature manipulation was successful in increasing the sensory thresholds.

	Tactors (Standing)		**Biothesiometer (Supine)**	
	F	**p-Value**	**F**	**p-Value**
Foot	1.542	0.216	0.43	0.513
Location	0.758	0.385	0.172	0.679
Temperature Condition	21.557	<0.001*	64.079	<0.001*
Foot * Location	0.117	0.733	0.097	0.756
Foot * Temperature Condition	0.041	0.989	0.329	0.805
Location * Temperature Condition	0.185	0.906	0.270	0.847
Foot * Location * Temperature Condition	0.256	0.857	0.147	0.931

* p<0.05

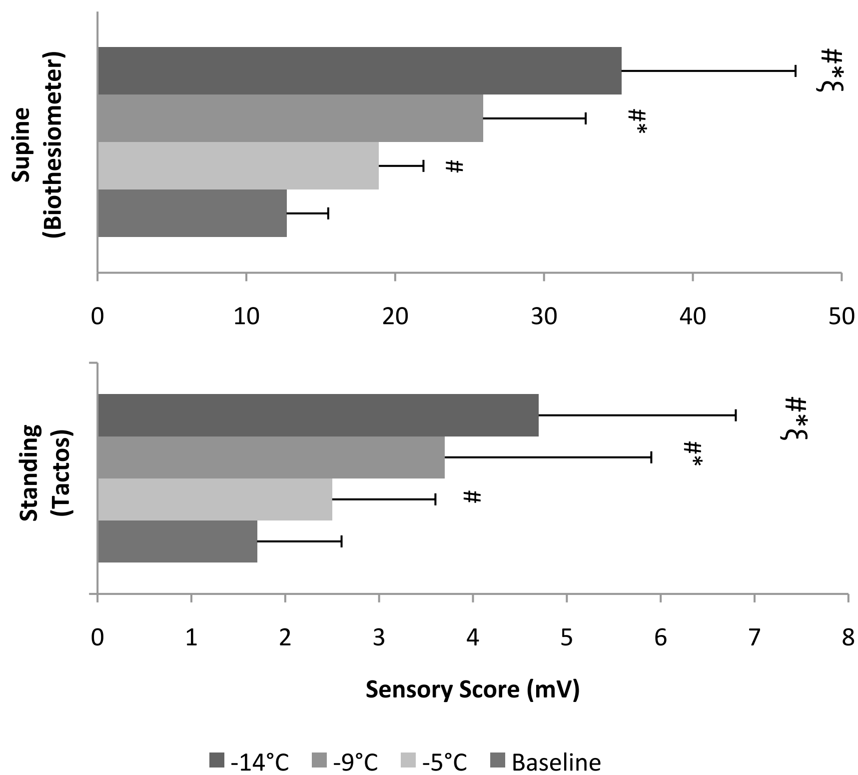

Figure 6.2: Impact of Cooling the Feet on the Sensory Threshold: Measurements are from both supine (Biothesiometer) and standing (tactors) postures. Differences in the magnitudes of sensory scores (mV) are due to different devices. These plots DO NOT indicate that the feet are less sensitive in the supine position than in standing. # > than baseline, * > Baseline-5, ξ > than Baseline-9, bars represent mean + 1 SD.

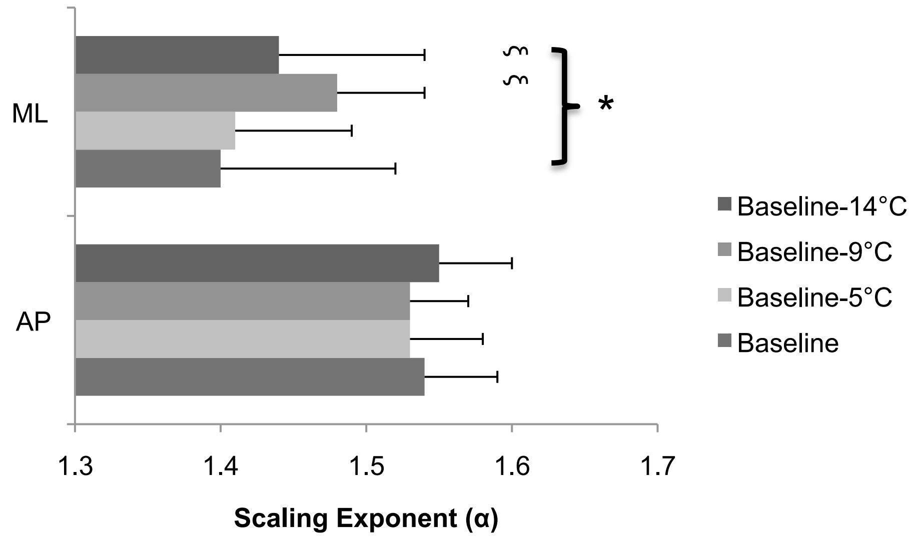

Figure 6.3 α-Exponents of DFA analysis: Change in the scaling exponent due to a change in the skin temperature. Bars indicate Mean + 1 SD. Results show a temperature effect for the scaling exponent in the ML COP fluctuations. Additionally the two coldest temperatures Baseline-9 and Baseline-14 both exhibited significantly greater α-values than the baseline temperature. *Indicates a main effect for skin temperature condition. ξ indicates a reduction from baseline $p<0.05$.

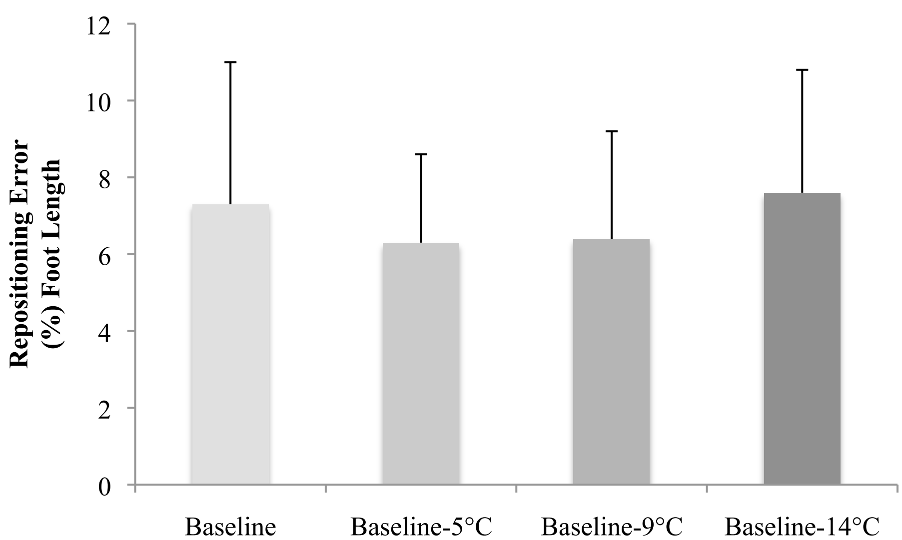

Figure 6.4: Impact of Cooling the Feet on Repositioning Error. The results here are for mean + 1 SD of the error in repositioning due to changes in skin temperature. There was no temperature effect.

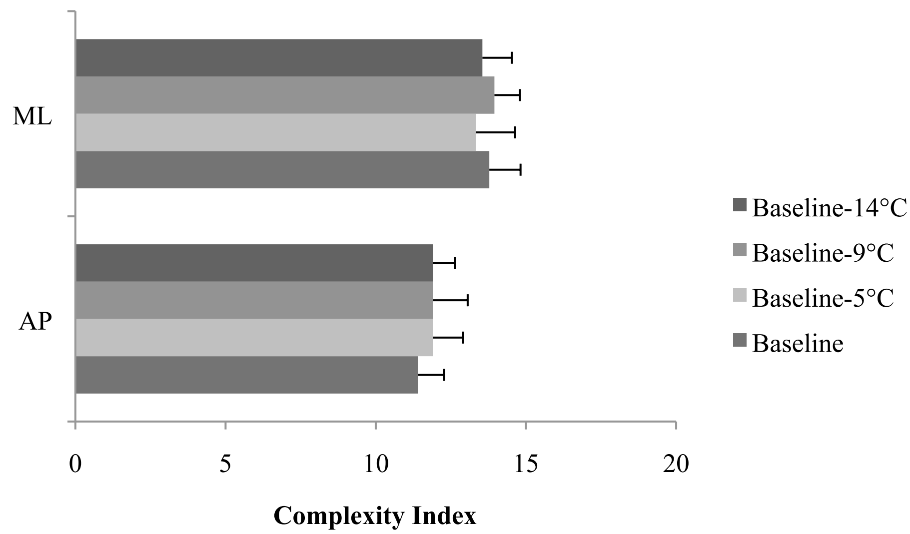

Figure 6.5: Complexity Indices. Bars identify Mean + 1 SD. The results of the ANOVA model indicate that there was no effect of temperature condition on the C_I in either that AP or ML plane of the COP fluctuations.

6.4 Discussion

The purpose of this study was to examine the effect of cooling the plantar surface of the feet on the ability to detect external vibrations applied to the skin, the control of posture, and perceived body orientation. Incrementally cooling the feet was found to increase the sensory thresholds of the feet in both sitting and standing (Figure 6.2, Table 6.1). Reductions in skin temperature increased the constraint of ML COP fluctuations, identified by an increase in the scaling exponent, with a shift toward α-values of 1.5—indicating that reductions in cutaneous sensation have a direct impact on the control of upright standing. However, the changes in skin temperature did not impact the perception of upright standing or the complexity index, $C_{I.}$

Cooling the feet 9°C conferred a ~100% increase in the sensory threshold, which is similar to the differences between individuals with and without multiple sclerosis (Remelius et al., 2012). Furthermore, Lowery et al. (2013) reported that cooling the skin

impacts all cutaneous sensory receptors in a uniform manner, thereby confirming cooling as a viable method to instantiate generalized sensory impairment. We thus identify cooling of the skin as a direct means of eliciting clinically relevant levels of sensory deficit in healthy individuals. This manipulation will therefore allow a direct examination of the relationships between cutaneous sensory loss and both the perception and control of upright standing while avoiding the confounding factors and comorbidities that often accompany sensory loss in clinical populations.

Lowering the skin temperature significantly increased the scaling exponent (α) of the ML COP (Figure 6.5), suggesting an increase in the constraint of the COP fluctuations as the feet are cooled. However, the entire range of scaling exponent (α) observed in both the AP and ML COP time series was near that of Brownian noise (~1.5), indicating that all of the observed postural fluctuations are highly constrained (Duarte & Sternad, 2008). The α-values reported here are similar to those previously reported in the literature for the same condition (quiet standing with eyes closed) (Kim et al., 2008). Importantly, those values were shown to be significantly elevated compared with values seen when vision remained intact, which exhibited α-values near 1.0 (Kim et al., 2008). These results suggest that the occlusion of vision in the current experiment may be driving the high level of postural constraint, which may in turn, be negating the efficacy of MSE for identifying differences in the control of COP due to skin cooling. This interpretation is supported by the work of Collins & Deluca (1995) who suggested that the occlusion of vision increase the stiffness of the musculoskeletal system by increasing the gain of non-visual feedback systems involved in the control of posture. The effective stiffening of the musculoskeletal system during visually-occluded postures likely impacts

postural control in ways that do and do not depend on feedback (closed- and open-loop control, respectively) (Collins & De Luca, 1993, 1995).

The increase in baseline stiffness results from a lack of adequate information about the postural state. This lack of information about the current state, which is used to govern open-loop processes, appears to result in postural fluctuations that are highly regulated at short time scales and then have large corrective fluctuations when an individual perceives instability. Postural corrections based on open-loop control likely occur on short time scales (<750 ms) as they are brought on by a continual assessment of the current state, whereas closed-loop processes occur at longer time scales (>750ms) (Collins & De Luca, 1993). The closed-loop, or feedback-based, control of posture relies on the integration of information from many sensory sources; this information, collected in parallel, is then used to correct postural disturbances. The weighting of the different sources of feedback appear to be based on the reliability of information collected from various sensory mechanisms, e.g., cutaneous sensory receptors, stretch receptors, and vestibular function (Polastri et al., 2012).

The DFA and MSE analyses performed in this study examine different ranges of time scales, with MSE focusing on short time scales and DFA spanning a much larger range. This difference is a function of the amount of data necessary to calculate values contributing to the respective analysis; at least 200 data points must be present for each MSE time scale, while only four are needed for DFA. The range of time scales examined by MSE, and the lack of change, suggest a uniform state of the open-loop postural control; while the changes in the scaling exponent, measured over a wider range of time

scales, suggest that cooling the feet impacts the closed-loop, feedback based, control of posture.

In the present study, occluding vision appears to elicit a uniform open-loop state of postural control, identified by the lack of change in the MSE analysis, and a high level of constraint in both the open- and closed-loop control of posture, indicated by α-values near 1.5 (Kim et al., 2008) across all temperature condition. Despite this high level of constraint the results presented here indicate that the reduction of skin temperature and accompanying reduction in cutaneous sensation further constrain the ML COP fluctuations. The inclusion of longer time scale fluctuations (>210 ms) in the DFA analysis identifies that impairing cutaneous sensation, through cooling the skin, impacts the closed-loop, feedback based, control of quiet upright standing. The changes in the long time scale postural fluctuations are in agreement with Collins and Deluca's (1993) model of postural control, where impairing cutaneous sensation impacts the closed-loop feedback-based control of quiet upright standing.

The factors that influence participants' ability to perceive body position as the feet are cooled are less clear. Incremental cooling of the skin did not appear to change the perception of postural orientation. This result differs from previous findings (Fujiwara et al., 2003); however, this contrast may be due to the difference in the amount the feet were cooled, with the current study cooling the feet less severely than in previous work. It is possible that when cutaneous sensation is only partially diminished, healthy individuals are able to successfully reweight the sources of sensory information in order to maintain an acute awareness of body position, even in the absence of vision.

A limitation to this work is that the sequence of the skin temperatures was from warmest to coolest. This stepwise procedure was chosen because the impact of cooling the skin on cutaneous sensory function is well understood (Lowrey et al., 2013), while the impact of warming and then recooling the skin on sensory function is not well understood. The choice to sequentially decrease skin temperature in a stepwise manner, while possibly introducing a learning effect across the trials, allows us to ensure that skin temperature was manipulated in a manner that allowed us to predict the underlying neurological impact.

6.5 Conclusion

The results of this study indicate that cooling the plantar surface of the feet is an effective way to experimentally induce cutaneous sensory loss in healthy individuals, to a level similar to that seen in individuals with clinical levels of sensory loss. This reduction in sensation appears to have the effect of constraining ML COP fluctuations such that the more cutaneous sensation is reduced, the greater the constraint. These changes appear to be occurring at longer time scales, indicating that reducing cutaneous sensation impacts the closed-loop, feedback based, control of posture. Though the occlusion of vision had a uniform impact on the open-loop control of posture, the results also indicate that occluding vision may have also impacted the closed-loop control of posture, identified by scaling exponent values near 1.5 in all temperature conditions. Therefore, further exploration of how somatosensory loss impacts both the open and closed loop control of posture should be done with vision left intact.

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CHAPTER VII

THE IMPACT OF STOCHASTIC RESONANCE ON THE PERCEPTION AND CONTROL OF UPRIGHT STANDING

Abstract:

Applying subsensory mechanical vibrations to the skin through stochastic resonance (SR) has been shown to elicit improvements in detecting external stimuli and controlling upright standing. The purpose of this study was to identify if SR improved the perception and control of upright standing during temperature-mediated cutaneous sensory knockdowns. Twelve healthy females aged 21-40 years underwent sensory and postural testing at normal skin temperature as well as 10°C and 14°C below this temperature, with and without SR applied to the soles of the feet. Perception of postural orientation was assessed by the ability to recreate a prescribed posture. Fluctuations in postural center-of-pressure during quiet upright standing were examined with both multiscale entropy and detrended fluctuation analysis (DFA) for the assessment of postural control. We found that SR enhanced the perception of body position, identified by a reduction in repositioning error. Contrary to previous findings, SR did not elicit changes in complexity of quiet standing, indicating no change in the control of upright standing. Additionally, we saw no impact of SR on the DFA scaling exponent, but reducing the skin temperature did have the effect of increasing the value of the scaling exponent toward 1.5. In fact, all center-of-pressure fluctuations exhibited scaling exponent values near 1.5, indicating a highly constrained system. The occlusion of vision may constrain postural fluctuations in a manner that obsecure the positive (SR) and

negative (cooling) influences on sensation. The results of this study suggest that, with vision occluded, SR improves the perception of postural orientation but has no impact on the control of quiet standing when cooling the skin experimentally impairs sensory function.

7.1 Introduction

Impairment of cutaneous sensory function in the feet is associated with many clinical conditions and has been associated with balance loss and increased fall risk (Menz et al., 2006). The application of subsensory white-noise signals to the skin, known as stochastic resonance (SR) (Benzi et al., 1981), has been shown to improve both sensory function (Collins et al., 1996b; Collins et al., 2003) and the control of posture (Priplata et al., 2003; Priplata et al., 2002; Priplata et al., 2006). Furthermore, these SR-related changes have been reported in a wide range of populations: young and old able-bodied adults (Priplata et al., 2003; Priplata et al., 2002), those with diabetes or stroke (Priplata et al., 2006), and older individuals with a history of falls (Costa et al., 2007). The manner in which SR manifests improvements in the control of posture is thought to be through augmenting cutaneous sensation. However, the way and degree to which SR can overcome the effects of cutaneous sensory impairments in order to improve postural control remains unclear.

Individuals with cutaneous sensory loss stemming from diabetes, aging, or multiple sclerosis often experience other comorbidities that can alter the control of posture and increase fall risk, such as decreased central motor drive (Ng, Miller, Gelinas, & Kent-Braun, 2004), chronic and acute fatigue (Van Emmerik et al., 2010), and decreased muscular power (Chung et al., 2008). The existence of these comorbidities makes it difficult to identify the isolated impact of cutaneous sensory function on the control of posture. Therefore, eliciting clinical levels of sensory loss in otherwise healthy individuals would allow for a direct assessment of the efficacy of SR to enhance

cutaneous sensory function, and the impact of this improvement on the perception and control of posture.

Moderately cooling the skin on the plantar surface of the feet has been shown to impair cutaneous sensation to levels observed among individuals with in clinical disorders (Chapter 6). Cooling brings about diminished cutaneous sensation through a decrease in neural activity across all types of cutaneous sensory receptors (Lowrey et al., 2013). These changes in sensory function in response to cooling appear to increase the cutaneous sensory thresholds, that is, the amplitude of external stimuli needed prior to detection (Billot et al., 2013; Fujiwara et al., 2003; Weitz, 1941, 1942). Reductions in sensory function due to cooling the skin also appear to elicit losses in the control (Billot et al., 2013) and perception (Fujiwara et al., 2003) of posture. In Chapter 6, we reported that reducing the temperature of the skin by at least 9°C increased cutaneous sensory thresholds to levels observed among persons with multiple sclerosis (Chapter 6; Remelius et al., 2012). Furthermore, cooling the skin also increased the DFA scaling exponent of medial-lateral postural fluctuations toward a value of 1.5. Postural dynamics that exhibit scaling exponents in this range are thought to be a result of a system under a high level of constraint. That is, there is a reduction in the dynamic processes that underlie the postural control mechanisms (Duarte & Sternad, 2008). Furthermore, a scaling exponent value of 1, representing pink (or 1/f) noise, is thought to be representative of systems that display a high level of complex interactions of the underlying processes governing the control of posture indicative of flexible and adaptable dynamics (Duarte & Sternad, 2008; Kim et al., 2008).

Stochastic resonance has been shown to enhance non-linear signaling in neural circuits (Collins et al., 1995a, 1995b; Collins et al., 1996a). These SR-mediated changes in neural activity are, in turn, thought to improve the detection of vibratory stimuli (Collins et al., 1996b; Wells et al., 2005) as well as the control of posture. It is often suggested that the mechanism by which postural control is enhanced is through augmented cutaneous sensory sensitivity (Costa et al., 2007; Priplata et al., 2003; Priplata et al., 2002; Priplata et al., 2006). While this pathway to postural improvements seems plausible, there have been no studies that directly address if SR can compensate for controlled reductions in cutaneous sensation. Therefore, isolating the impact of SR on the perception and control of posture during experimentally induced somatosensory loss will elucidate the capacity of this promising aid to improve these aspects of posture.

As SR appears to impact the processes that contribute to the successful control of upright standing, selecting methods that allow for the assessment of intrinsic dynamics of the postural fluctuations is important. The application of SR and its proposed method for enhancing postural control, improved access to external information as well as enhanced (ex)propriception, should result in an increase in complexity and a reduction of constraint in the control of posture. Multiscale entropy (MSE) and detrended fluctuation analysis (DFA) are measures that allow for the identification of changes in the complexity and constraint of postural fluctuations, respectively. Quantifying complexity allows for an assessment of the physiological interactions that underlie integrative behaviors; within a system, a reduction of complexity is indicative of a reduced number of functional interactions in the system. DFA allows for the quantification of how fluctuations on short time scales impact fluctuations that occur over longer time scales, with a deviation from

1/f scaling, where f is the frequency of the signal, being indicative of a constrained physiological system. This constraint is due to a breakdown in the interactions of the system such that processes that occur on short time scales no longer influence those that occur on longer time scales.

MSE has been shown to demonstrate reductions in the complexity of postural control among individuals with cutaneous sensory loss compared to individuals free of clinical impairment (Costa et al., 2007). Additionally, we have reported that DFA was able to identify increases in constraint of the postural fluctuations, identified as an increase in the scaling exponent (Chapter 6; toward a value of 1.5) in response to cooling the feet and the associated reduction in cutaneous sensation.

The purpose of this study was to examine if applying SR to the plantar surface of the feet improves the perception and control of posture when cutaneous sensation was impaired via cooling the skin. Specifically, we aimed to investigate whether, when cutaneous sensation was reduced to clinical levels via a cooling of the feet, applying SR to the soles of the feet would improve: 1) the perception of postural orientation, and 2) the control of posture. We hypothesized that, compared to trials that did not apply SR, the application of SR to the soles of the feet would have: 1) a reduction in the repositioning error, 2) an increase in the complexity index and decrease in constraint (α-values approaching 1.0). Finally, we hypothesized that SR would improve postural perception, increase complexity and reduce the constraint of the COP position time-series in a baseline-dependent manner, such that the more the skin is cooled below baseline, the more SR would improve performance.

7.2 Methods

7.2.1 Participants

Twelve female participants were recruited from the University of Massachusetts and surrounding communities (29.4 (4.9) *yrs*, 1.65 (0.07) *m*, 57.7 (20.3) *kg*; mean (one standard deviation)). Participants provided written informed consent prior to study participation. The Institutional Review Board at the University of Massachusetts Amherst approved all procedures. All participants reported being free from cutaneous sensory impairment, injury, neural degeneration, cognitive deficits and visual impairments.

7.2.2 Experimental Procedures

Participants wore comfortable clothes for all procedures, which involved completing one trial at each temperature, SR, and postural condition. Testing was performed at three different skin-temperature conditions: baseline (BL, less than 1°C change in 10 minutes), as well as 9.9°C and 14°C below baseline (BL-10 and BL-14, respectively). We have previously shown that decreasing the skin temperature by these amounts elicits clinically relevant increases in the cutaneous sensory thresholds (Chapter 6). Individuals feet were placed on ice for 2 minutes in order to decrease the skin temperature to the targeted temperatures, after this period of cooling skin temperature was reassessed and additional cooling occurred as necessary to reach target temperatures. Skin temperatures were assessed between tasks that took more than 1 minute to complete; if the feet warmed more than 1°C, further cooling was used to maintain the target skin temperature. Skin temperature was assessed with an Exergen DX1001 infrared thermometer (Exergen Corp., Watertown, MA).

Sensory function was assessed in both supine and standing postures. In both postures, sensory thresholds were measured on the plantar surface of the left and right feet at approximately the 3rd metatarsal head and the center of the heel. In the supine posture, participants were asked to identify the onset of vibration as the oscillation (120 Hz) amplitude of the Biothesiometer probe was gradually increased. This value was used to ensure that the temperature manipulation elicited clinical levels of sensory loss (Remelius et al., 2012). During quiet standing, sensory function was assessed by C-2 tactors embedded in the soles of custom modified sandals (Teva, Deckers Outdoor Corporation, Goleta, CA), using a 4:2:1 technique (Chong & Cros 2004). In the 4:2:1 method for determining sensory threshold the 30-350 Hz (white noise) signal amplitude was increased from the lowest level four levels at a time until the participant was able to detect it. The signal was then decreased two levels at a time until the participant was unable to detect it. Finally, the signal was modulated one level at a time until neighboring vibrations produced responses where one was identifiable and the other was not. With both devices, sensory threshold was identified as the lowest voltage at which participants could detect vibration.

Subsequently, participants completed postural tasks at all three temperature conditions, from warmest to coldest, for the assessment of the perception and control of posture (Figure 7.1). All postural tasks were performed on one AMTI force platform (AMTI Corp., Watertown, MA), surrounded by 11 Qualysis cameras (Qualysis, Gothenberg, Sweden); kinetic and kinematic data were collected at 100 Hz in Qualysis Track Manager (Qualysis, Gothenberg, Sweden). Trials with and without SR were presented in random order so that participants were blinded to the trials where SR was

applied (Appendix D). The SR signal was applied during the assessment of postural reorientation and quiet upright standing tasks and consisted of a 30-350 Hz white noise profile with an amplitude of 80% of the standing sensory threshold, an amplitude that has previously been shown to improve stimulus detection (Wells et al., 2005). During all posture trials, participants wore an eye-mask to occlude vision and noise canceling headphones to mute the soft audible buzz emitted by the tactors. Vision was occluded in order to increase reliance on cutaneous sensory information. Polastri et al. (2012) suggest that a large degree of intersensory reweighting can occur; when the reliability of one modality is compromised the reliance is shifted toward a more reliable mode. Therefore, by eliminating visual information, individuals will shift their reliance on cutaneous sensation in the control of upright standing.

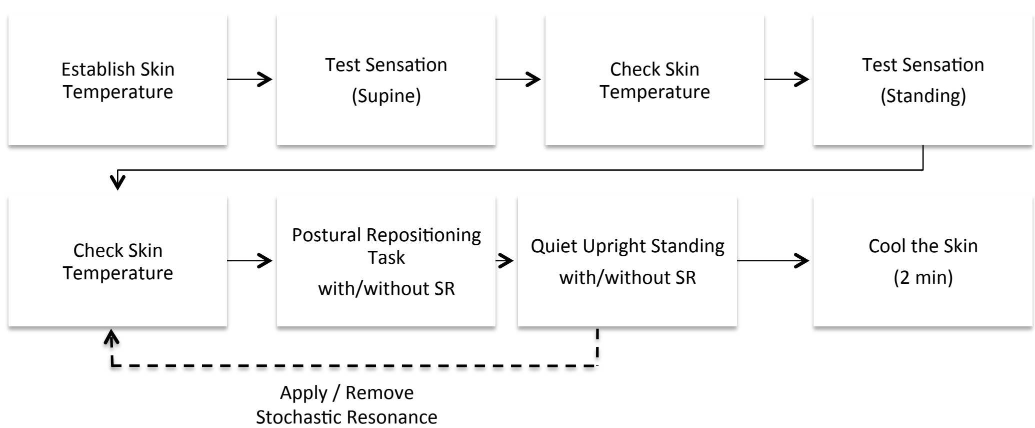

Figure 7.1: Procedure for Sensory and Postural testing. The sequence used for the impact of SR on the perception and control of posture. Participants underwent one assessment of sensation, sitting and standing at each temperature. The perception and control of posture were quantified by the postural repositioning task and quiet upright standing, respectively. The application of SR was randomized such that participants were blinded to the trials that applied SR to the soles of the feet.

A postural repositioning task was used to assess the perception of posture. During this task, participants were coached into a lean that placed the COP 60% of the foot-length forward of the heel through rotation about the ankles. This posture places the COP forward of that which normally occurs in quiet standing (~45% of the foot length forward from the heel) (Fujiwara et al., 2003). This position was identified by the experimenter, who viewed the net ground reaction force in real time in the data collection software and verbally instructed participants to "lean forward, backward, left or right" until the vector passed through a target placed such that the center was between the feet, 60% of the foot length forward of the posterior border of the feet (Figure 3.3). Participants were instructed to maintain this position for 5 s while gaining perceptual awareness of their postural orientation. Participants then sat for at least 5 s prior to recreating the coached posture to the best of their abilities. This period of sitting between coached and recreated postures was included to wash out the coached posture prior to asking the participant to recreate it. Once participants felt they had recreated the coached position, they verbally notified the examiner, at which point they were instructed to maintain it for 5 s. In both the positioning and repositioning task, COP position was collected for 5 s, with the first 3 s used to assess the ability to recreate the posture. To ensure that shifts in foot position, between the coached and recreated postures, did not impact the measurement of repositioning error, passive markers were placed approximately at the midpoint of the posterior side of the heels and COP positions were calculated relative to the midpoint of heel markers.

The control of posture was assessed during quiet standing. Participants were instructed to stand with their feet at a comfortable width and arms at their sides. The quiet standing posture was maintained for 40 s, during which COP position was recorded.

7.2.3 Construction of Dependent Variables

As was done in Chapter 6, the perception of postural orientation was assessed by calculating the repositioning error, defined as the differences in the COP location between the reference and reproduced leans, relative to the midpoint between the heels. This is calculated as:

$$repositioning\ error = \frac{\sqrt{\left(\bar{x}_{rep} - \bar{x}_{ref}\right)^2 + \left(\bar{y}_{rep} - \bar{y}_{ref}\right)^2}}{footlength} \qquad \text{Eqn. 7.1}$$

where $\bar{x},\bar{y}_{\text{rep}}$ and $\bar{x},\bar{y}_{\text{ref}}$ are the 3 s averages of the x and y positions in the reproduced and reference positions, respectively. The repositioning error, as a percent of foot length, was used as the dependent variable in statistical analysis.

The control of posture was assessed by MSE and DFA of the anterior-posterior (AP) and medial-lateral (ML) COP position time series (Busa, Chapter 6). The area under the sample entropy (S_E) vs. time scale curve was computed over 7 time scales, ranging from 30-210 ms. The MSE procedure consisted of calculating the S_E values (Richman & Moorman 2000) of the coarse-grained time series and numerically integrating the S_E vs. time scale curve to calculate the value of the complexity index (C_I). (For details, see Costa et al. (2002) and Goldberger et al. (2000), as well as Chapter 3 (section 3.4.2.1)). S_E parameters were set to r=0.15 and m=2.0. C_I was used as the dependent variable in statistical analysis.

DFA was also assessed for COP position time-series during quiet standing, with non-overlapping windows of sizes 4 to N/4 used to assess the linearly-detrended fluctuations, where N is the total number of samples in the time series (Chapter 6). This corresponds to window sizes ranging from 40 ms – 10 s. The slope of the resulting log/log plot of *n vs. F(n)* was taken as the value of the scaling exponent (α) (Peng et al., 1995). Scaling exponents were used as dependent values in statistical testing.

7.2.4 Data Reduction

Following the procedures outlined in Chapter 6, outliers were defined as any point x, where x<25th percentile-1.5*IQR or x> 75th percentile+1.5*IQR (where IQR is the interquartile range), and were removed from all COP position time series prior to analysis. 4th order recursive Butterworth filters with cutoffs tailored to the specific analysis were used to filter the data. For (re)positioning trials, a lowpass cutoff of 4 Hz was used, while cutoffs for quiet standing trials used for MSE analysis were 2 to 20 Hz band-pass. The quiet standing time series used for DFA analysis was not filtered. The time series was not filtered for DFA analysis, as high pass filtering this data has been shown to remove long-range correlations. All filters were applied using custom written MATLAB software (Mathworks, Natick, MA).

7.2.5 Statistical Analysis

The impact of SR for improving the perception and control of posture was evaluated by separate linear mixed model analyses of variance (ANOVA) with skin temperature condition (BL, BL-10 and BL-14), and the presence or absence of SR as

fixed factors and the repositioning error, complexity index, and scaling exponent (α) as dependent variables. If main or interaction effects were found, pairwise t-tests were used to assess where specific differences lie.

Additionally, if main effects were seen in the ANOVA models, the nature of the relationship of skin temperature with changes in the dependent variables due to SR was explored. This was done by examining first, second and third order regressions. For example, in the case where significant effects were observed for repositioning error (*RE*), the third order regression equation is as follows:

$$RE_{SR} - RE_{noSR} = \beta_1(t_{below\,baseline})^3 + \beta_2(t_{below\,baseline})^2 + \beta_3(t_{below\,baseline}) + \beta_4 + \varepsilon \qquad \text{Eqn 7.2}$$

where $t_{below\ baseline}$ is the reduction in skin temperature below baseline. In this model, positive relationships indicate an improvement in response due to SR with decreases in skin temperature. The evidence ratio from the corrected Akaike Information Criterion (cAIC) weightings was used to compare models (Wagenmakers & Farrell, 2004). The cAIC uses the principle of parsimony to balance goodness of fit against model complexity.

Significance was assessed at $\alpha=0.05$ for all statistical tests, and trends identified as $0.05<p<0.10$.

7.3 Results

7.3.1 SR and the Perception of Body Position

Applying SR to the plantar surface of the feet decreased the repositioning error ($p=0.012$, Table 7.1, Figure 7.2). Additionally, there was no interaction effect between SR or skin temperature condition. Regression analysis, done to address between-subject

variations in skin temperature, indicated that the more the skin of the feet was cooled, the more SR decreased the repositioning error. Comparison of 1st, 2nd, and 3rd order regression models revealed that the 1st order (linear) model provided the best fit to the data (Figure 7.2, Table 7.2, $F_{22,1}$=5.193, p=0.03, r^2=0.19, cAIC Weighting = 0.79). Furthermore, there was not an effect of cooling the skin on the repositioning error (Table 7.1).

Table 7.1: Effect of Skin Cooling and Stochastic Resonance on the Perception of Body Orientation and Control of Posture. Repositioning Error, Complexity Index and Scaling Exponent for both the anterior-posterior (AP) and medio-lateral (ML) directions.

	Repositioning Error		Complexity Index				Scaling Exponent			
			ML		AP		ML		AP	
	F	p	F	p	F	p	F	p	F	p
Temperature	.556	.576	.941	.395	1.309	.277	8.410	.006	.208	.737
Stochastic Resonance	6.702	.012*	.173	.679	.048	.828	.017	.899	.508	.491
Temp * SR	.306	.737	.542	.584	1.382	.258	.890	.425	.389	.683

*Indicates a Significant Effect.

Table 7.2: The Relationship Between Reductions in Skin Temperature and Repositioning Error. Evaluation of 1st, 2nd and 3rd order fits of change in skin temperature (below baseline) to changes in repositioning error due to SR.

	cAIC	Change in cAIC	Relative Likelihood	Akaike Weight
Linear	-84.298	0	1	0.79421136
Quadratic	-81.597	2.701	0.259110673	0.20578864
Cubic	*			

* Indicates that a cubic order fit could not be made as the coefficient of the 3rd order term was zero.

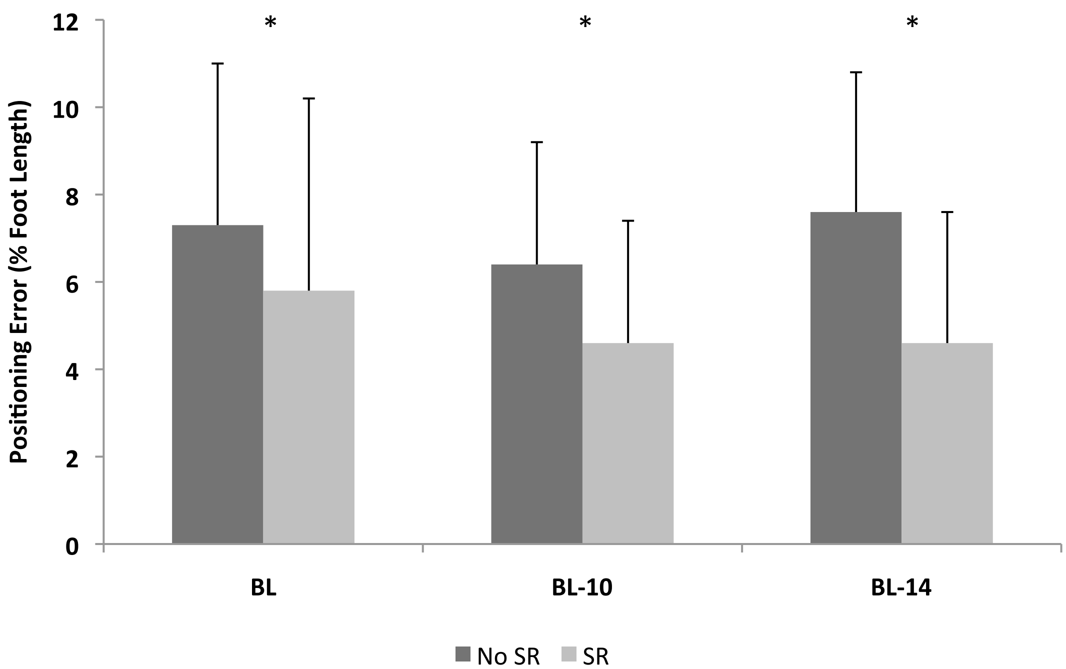

Figure 7.2: Repositioning Error: The impact of SR on improving the ability to reposition the body. Values closer to 0 indicate a better ability to reposition the body. Repositioning error was measured at the baseline skin temperature (BL), 10 and 14°C below the baseline temperature (BL-10 and BL-14, respectively). *Reduction in error compared to No SR condition. Bars represent group means; error bars represent 1 standard deviation. * Indicates a difference between SR and NO SR at p<0.05, bars represent mean + 1 SD.

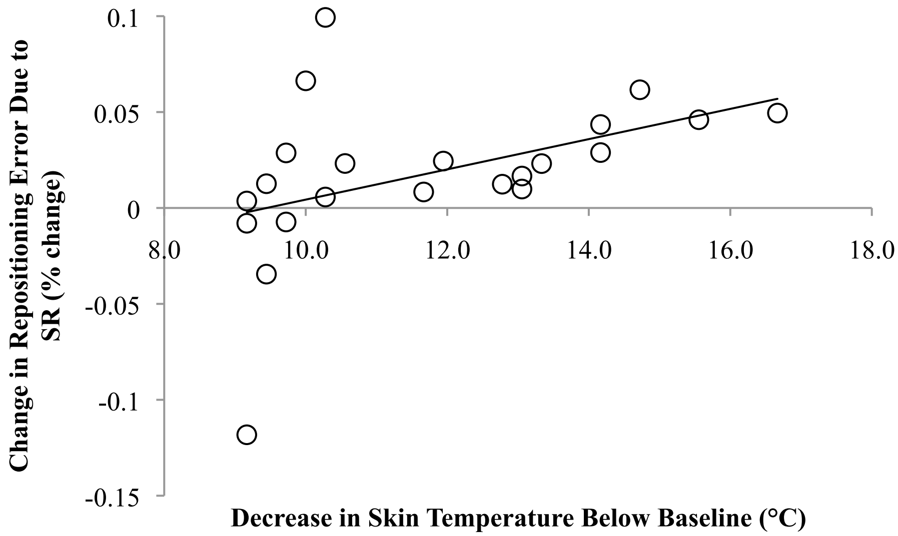

Figure 7.3 Regression of the Change in Skin Temperature vs. Change in Repositioning Error. Values > 0 indicate improvement in the ability to reposition the body. r^2=0.19, p=0.033, $F_{22,1}$=5.193. The corrected Akaike information criteria (cAIC) indicates that the linear regression model exhibits a 3.85 times better fit than 2nd order model. The second and third order models were identical as the cubic coefficient exhibited a value of 0.

7.3.2 The Impact of SR on the Complexity of Quiet Standing

The complexity index C_I of the COP position time series in the AP and ML directions did not demonstrate differences between conditions with and without SR (Figure 7.3, Table 7.1). Nor were any changes observed in the scaling exponent (α) of the AP and ML COP time series between the conditions with and without SR (Figure 7.4, Table 7.1). However, as we have previously demonstrated (Chapter 6), cooling the feet had a significant effect of increasing the scaling exponent of the ML COP position (Table 7.1, Figure 7.4).

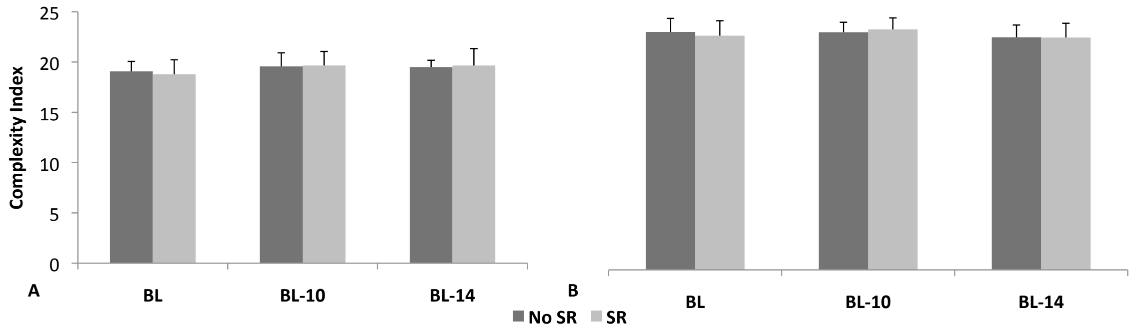

Figure 7.4 Impact of SR on the Complexity of Quiet Standing. A) Complexity of the Anterior-Posterior (AP) center of pressure (COP) position time series. B) Complexity of the Medial-Lateral (ML) COP position time series. Applying SR to the soles of the feet did not change the complexity index of either the AP or ML COP time series for any of the three skin temperature conditions. Bars represent mean + 1 SD.

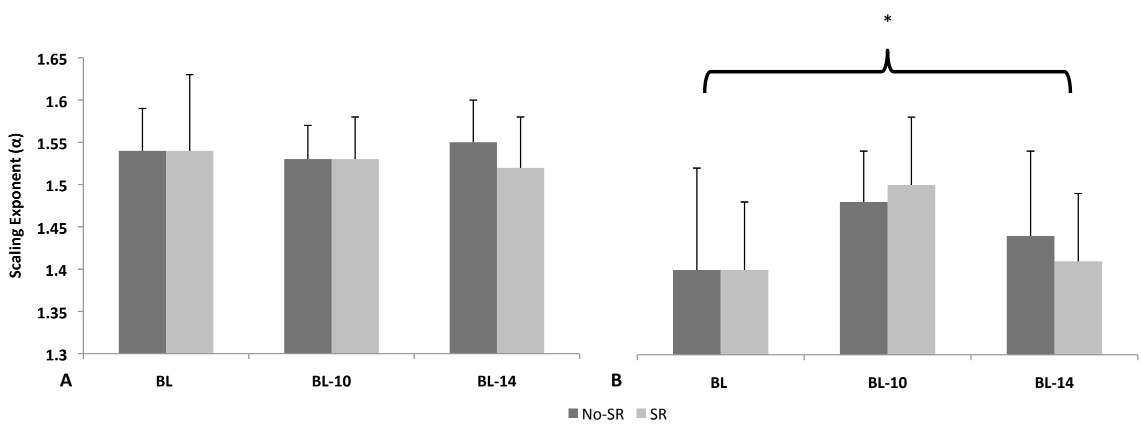

Figure 7.5: Impact of SR on the Scaling Exponent During Quiet Standing. A) Scaling exponent of the anterior-posterior (AP) center-of-pressure (COP) position time series. B) Scaling exponent of the Medial-lateral (ML) COP position time series. Applying SR to the soles of the feet did not elicit changes in the value of the scaling exponent in either the AP or ML direction. There was however a significant temperature effect of increasing the scaling exponent. *p<0.05 for an overall temperature effect, bars represent mean + 1 SD.

7.4 Discussion

The purpose of this study was to identify if SR improves the control of COP fluctuations and perception of postural orientation under both normal and impaired sensory conditions. The results indicate that SR improved the perception but not the

control of upright standing. Applying SR to the soles of the feet during experimentally induced reductions in cutaneous sensation enhanced the perception of body position, likely through the mechanism of improving the detection of external vibration with the feet (Wells et al., 2005). Regression analysis indicated that the more the skin was cooled, eliciting greater reductions in sensation, the more SR improved the perception of postural orientation (Table 7.1, Figure 7.2). However, SR did not appear to improve the control of postural fluctuations when the ability to detect external vibration was impaired via a cooling of the skin. This may have been due to the removal of vision, which has been shown to constrain postural fluctuations in a manner that are similar to what we would expect to observe when cutaneous sensation is impaired (Kim et al., 2008).

We have previously demonstrated that cooling the soles of the feet in healthy young individuals to 9°C below baseline is an effective means of increasing sensory thresholds to a level that mimics the sensory status of individuals with mild-to-moderate multiple sclerosis (Chapter 6) (Remelius et al., 2012). Using this insight to guide our experimental manipulations, we identify here that SR enhanced the perception of body orientation when sensory function was impaired, with greater effects of SR with increasing levels of sensory function impairment. This result is in accord with the work of Stephen et al. (2012) who reported that SR conferred a greater reduction in gait variability among those with the greatest impairment. These results suggest that SR-mediated enhancements in the detection of external vibrations have the potential to improve the perception of postural orientation among all persons with clinical sensory loss and likely confer the most benefit to individuals with greater sensory loss. While devices that apply SR signals to the soles of the feet appear to have the potential to

directly overcome clinical levels of sensory loss in otherwise healthy women, it remains necessary to identify just how much this type of aid improves the quality of life in individuals with pathologies that impact cutaneous sensation.

While the changes in perception of posture matched our hypothesis, we did not see the expected changes in the measures of postural control. That is, we did not see increases in the C_I or a significant change in the scaling exponent values toward a value of 1.0 (Table 7.1, Figures 7.3 & 7.4), both of which were predicted. These results suggest that applying SR to the soles of the feet neither increased the complexity of postural fluctations, nor removed constraint in postural fluctuations. The exact reason that SR was unable to improve the control of posture is unknown, but it appears that occluding vision may have impaired the ability to evaluate the impact of SR on the feedback-based control of quiet upright standing (Chapter 6).

The results of the DFA analysis support this claim; the values of the scaling exponents (α), which were near 1.5, point to a high level of constraint in the postural fluctuations (Kim et al., 2008). These values indicate that the physiological processes underlying the control of posture when vision is occluded are impacted, in that they exhibit a low degree of systemic flexibility (Collins & De Luca, 1993, 1995). Kim et al. (2008) tied the effects of vision to postural constraints, reporting significantly elevated scaling exponent values during standing with eyes closed, but a much lower level of constraint when participants stood with eyes open (α-values ~1). This fits within the framework set forth by Collins & DeLuca (1993, 1995) where the occlusion of vision serves to increase the stiffness of the musculoskeletal system. This increase in stiffness resulted in a reduction in the stochastic processes that underlie postural fluctuations. As

stochastic processes are impaired, the baseline capability of the system will be impaired in a manner that indicates a reduction in the ability of the system to respond to disturbances.

As increased musculoskeletal stiffness is a descriptor of the underlying state of the processes contributing to the control of posture, the lack of change in the MSE results suggest uniformity in the open-loop control of posture. As we observed an elevated value of the scaling exponent (~1.5), even in the baseline temperature condition, it appears that occluding vision impacts both the open- and closed-loop control of posture. Therefore, the changes observed in response to the step-wise cooling of the feet are likely in the closed-loop control of posture. As SR is thought to improve postural control through enhancing cutaneous sensation, used in the closed-loop control of posture (Collins & De Luca, 1993), it follows that the high level of constraint observed in the postural fluctuations may impact the ability of SR to improve the complexity of COP fluctuations.

The experimental manipulation of cooling the feet impacts the control of posture by constraining the postural fluctuations, identified by a shift in the scaling exponent toward a value of 1.5. The change in postural control observed as a result of the cooling is congruent with the model of postural control set forth by Collins and Deluca (1993), where we observe changes in the closed-loop, feedback-based control. The lack of observed change in the MSE analysis suggests that cooling the feet does not impact the short time scale (<250 ms), open-loop control of posture, which is also in agreement with the model put forth by Collins and Deluca (1993). According to this model we should have observed an improvement in the control of quiet upright standing when SR was applied to the feet.

The change in postural constraint that accompanies the occlusion of vision likely impairs the ability to properly evaluate if SR is able to improve the control of posture—to do so it will be important to assess SR in subsequent studies where vision is left intact. Furthermore, experiments that include vision will allow for the assessment of whether SR is able to improve the control of upright standing through the proposed mechanism of enhancing the ability to detect external information. This is an important step in understanding just how SR is able to impact the control of posture and further identify potential circumstances where SR will have the greatest impact.

In this study, the experimental choice to occlude vision was made with the intent of placing greater reliance on cutaneous sensory information. However, as our results are in conflict with previous reports that SR applied to the soles of the feet improved measures of postural control among individuals with cutaneous sensory impairments (Costa et al., 2007; Priplata et al., 2003; Priplata et al., 2002; Priplata et al., 2006), we conclude that occlusion of vision may have instead obscured the effect of both the temperature-mediated reductions and the SR-mediated enhancements in cutaneous sensation. Additionally, it is unclear how including multiple (re)cooling sessions, necessary to maintain constant skin temperature, may have impacted neural conduction. Therefore, to minimize confounding factors, the scope of this work was limited to only the vision occluded condition. Nonetheless, to identify just how much the occlusion of vision impacts the positive (SR) and negative (temperature) effects on postural control, these effects need to be examined when vision is left intact.

Another limitation of this work is that the sequence of the skin temperatures was from warmest to coolest. This stepwise procedure was chosen because the impact of

cooling the skin on cutaneous sensory function is well understood (Lowrey et al., 2013), while the impact of warming and recooling the skin on sensory function is not well understood. The choice to sequentially decrease skin temperature in a step-wise manner, while possibly introducing a learning effect across the trials, allowed us to ensure that we manipulated skin temperature in a manner that allowed us to control the underlying neurological impact.

7.5 Conclusion

Stochastic resonance appears to be a suitable method for improving the perception of postural orientation, and the more cooling of the feet impairs sensation, the more SR confers a benefit. Past research has shown SR to improve the control of posture; however, the occlusion of vision in our experimental design may have obscured our ability to observe these impacts. In the future, it will be important to identify if SR can counteract the impact of reduced sensation on the control of upright standing when vision is left intact.

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CHAPTER VIII

GENERAL DISCUSSION

8.1 Introduction

The purpose of this dissertation was to better understand the factors that influence the control and perception of upright standing. The approach taken here provides an initial exploration into how plantar forces, in weight bearing postures, impact the detection of external vibrations by the plantar surface of the feet, and if changes in plantar sensitivity affect the dynamics and perception of upright standing. The series of three experiments presented here explored these relationships by examining: a) how changes in posture, from supine to sitting to standing, impact the ability to identify external vibrations; b) how decreasing skin temperature impacts: the detection of these vibrations as well as the perception and control upright standing; and c) how applying stochastic resonance (SR) to the soles of the feet improves the perception and control of posture when plantar sensitivity is reduced in healthy individuals. The outcomes of this series of experiments indicate that weighting the feet reduces plantar sensitivity when external vibrations are applied to the feet—that is, as more weight is placed on the soles of the feet, they become less sensitive to external vibrations. Cooling the skin of the feet increases the threshold for detecting external vibrations. Cooling the skin also impacts the medial-lateral (ML) center of pressure (COP) fluctuations such that the cooler skin temperatures the more ML COP fluctuations are constrained. Finally, applying SR to the soles of the feet improves the perception of posture when the skin of the feet is cooled to

elicit reductions in vibratory threshold, and the more the skin is cooled, the more SR improves postural perception.

8.2 Conceptual Framework

The results of the studies that comprise this dissertation, along with other work on the integration of different sensory modalities, suggest a negative feedback structure that involves multiple sensory modalities for the control of posture (Figure 8.1). The sensory information used to formulate motor commands is always out of date; generating a model that has separate feedback controllers for each sensory modality will afford for the continual updating of the integrator with the most recent information, thereby allowing for a continual adjustment of motor commands. The framework used here differs from that of Collins & Deluca (1993) in that it recognizes that different sensory systems contribute information relevant to the control of upright standing on different time scales, and that by continually updating the integrator with the most salient information, individuals are able to best perform the task. In this schema, $state_0$ represents pseudo-initial conditions and results in initial motor responses, though these commands are updated continuously as new sensory information becomes available. The use of visual information in the control of upright standing is broken up into two states, one on short time scales (<210 ms) and another on long time scales (>210 ms). This short time scale response is indicative of an open-loop process and is considerably shorter than some models use for the time scale of open-loop processes (Collins & De Luca, 1993). This conservative classification of the open-loop control of posture is indicative of $state_0$.

This schema outlines a complete perception/action system, in particular, the influence of posture on cutaneous sensation and the impact of cutaneous sensation on posture in healthy young women. The circular nature of the relationship between posture and cutaneous sensation is represented by the loop which begins by identifying that the musculoskeletal system influences cutaneous sensation, and is completed when that cutaneous sensory information then feeds back to the integrator, which in turn specifies motor commands resulting in a musculoskeletal response. In the first study we identified that changing the amount of weight borne by the feet alters the ability to detect external vibrations. Additionally, we observed that changes in the ability to detect external vibrations, brought about by cooling the plantar surface of the feet, impacted the control of postural fluctuations, but not the perception of body position. The ability to position the body in space relies on expproprioceptive mechanisms, including all the types of sensory information identified in the schema: visual, vestibular, and haptic/cutaneous sensory; for the purpose of this schematic, expproprioceptive information is used specifically for the purpose of gaining awareness of body position in space. Following from the work of Jeka and colleagues, we know that if one mode of sensory information is made unreliable (Polastri et al., 2012), as we have done with cutaneous sensation in these studies, reliance on that mode is down-weighted and other sensory modes (e.g., stretch receptors and vestibular function) have increased reliance placed on them. The sensory redundancy that contributes to expproprioception likely allows for individuals to overcome the loss of cutaneous sensory information while still maintaining the ability to reposition the body. Furthermore, we observed an improvement in the ability to reposition the body when SR, which has been shown to enhance the detection of external

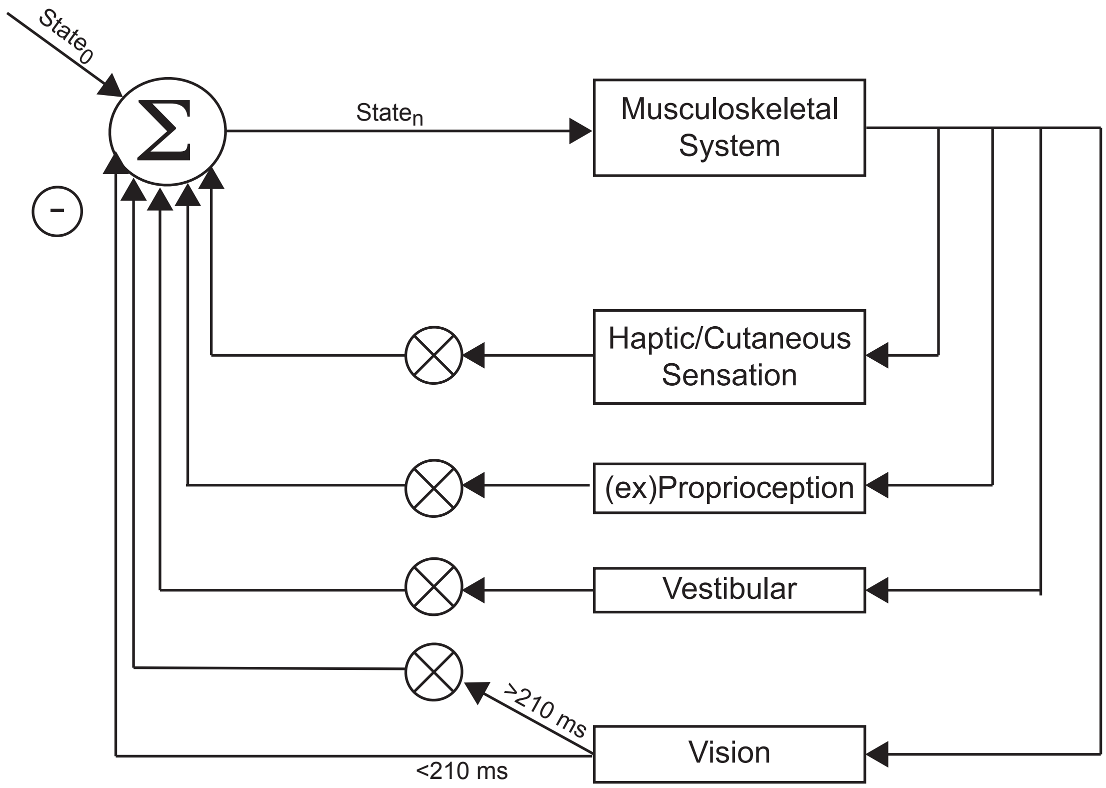

Figure 8.1: Control Schema. Integration of sensory information in the use of motor commands for the use of postural control, a negative feedback control system. Where ⊗ represent feedback controllers and Σ is the system integrator, combining all the sensory feedback in one negative feedback loop (-). Additionally, $state_0$ and $state_n$ represent the motor response to the initial sensory state, and updates to that state based on the most current sensory information.

vibrations (Collins et al., 1996b), was applied to the soles of the feet. The improved ability to reposition the body when SR was applied to the plantar surface of the feet suggests that increasing the ability to identify cutaneous sensory information, when accompanied with other exproprioceptive mechanisms, improves an individual's ability to reposition the body.

Quiet upright standing with vision occluded appeared to produce a uniform open-loop state, identified by a lack of change in complexity index between temperature

conditions, indicating that as the fidelity of cutaneous sensory information was degraded by cooling the skin of the feet, postural control was impaired as identified by a shift in the DFA scaling exponent toward a value of 1.5. Furthermore, SR signals did not have the intended effect of improving measures of postural control, though the observed improvement in the ability to reposition the body suggests that aids aimed at improving balance by enhancing the ability to detect external information are able to improve some aspects of upright standing.

8.3 Forces Under the Feet Impact the Ability to Detect External Vibration

The results of the first study of this dissertation revealed, in short, that changes in forces under the feet due to changes in posture impact the ability to detect externally applied vibrations. The changes in plantar force that accompany a shift from sitting to standing increase cutaneous sensory thresholds under both the fore- and rearfoot. However, the shift from supine to sitting, which confers a smaller change in the amount of weight than the shift from sitting to standing (~10 vs. 30% at each measurement site) elicited a trend for increased sensory threshold in the forefoot, but not in the rearfoot. This indicates that the cutaneous sensory thresholds of the forefoot are more sensitive to changes in weighting than the rearfoot. Furthermore, individuals appear to weight their feet in an asymmetrical manner; these small bilateral differences (~1-5% of body weight), however, were insufficient to elicit changes in healthy women in the ability to detect vibrations applied to the plantar surface of the foot. The results of this study provide a foundation for assessing the role of plantar pressure fluctuations in facilitating the detection of external information, suggesting that pressure fluctuations under the feet

may facilitate the detection of external information by shifting the location of areas of low force. As we demonstrate here, reducing the load under the feet improves the detection of external vibrations. Riccio and colleagues have suggested that center of pressure (COP) variability plays a key role in the identification of external information (Riccio, 1993; Riccio, Martin, & Stoffregen, 1992; Riccio & Stoffregen, 1991). Nevertheless, the way in which COP variability links to the pressure patterns and distributions under different portions of the feet remains unknown. Further investigation is necessary to identify how a reduction in COP variability (Riccio, Van Emmerik, & Peters, 2001), frequently observed among individuals with clinical sensory loss, impacts the detection of external information.

8.4 The Influence of Skin Temperature on the Ability to Detect External Vibrations

The results of the second study of this dissertation indicate that cooling the plantar surface of the feet is an effective way to experimentally induce cutaneous sensory loss in healthy individuals to a level similar to that found in clinical populations, such as individuals with multiple sclerosis (MS). The results of the detrended fluctuation analysis (DFA) suggest that reductions in sensation appear to have the effect of constraining ML COP fluctuations, such that the more the temperature of the skin is cooled the greater the constraint. This increase in constraint indicates that individuals may have a reduced ability to adapt their postural fluctuations to challenges. The nature of the observed scaling exponent values indicate that cooling the feet alters ML COP fluctuations in a manner such that short time scale fluctuations do not correlate to longer term fluctuations, which are congruent with Brownian motion. The results of the DFA analysis, coupled

with a lack of difference in the complexity indices in response to cooling the skin, suggest that the changes in the control of posture brought about by a cooling of the skin occur at time scales which utilize cutaneous sensory feedback (closed-loop) in the control of posture. The nature of the changes occurring at long time scales indicates that reducing cutaneous sensation impacts the closed-loop control of posture. However, regardless of temperature condition, DFA analysis identifies a high level of constraint in the COP fluctuations.

The high level of constraint observed here is consistent with other reports of quiet standing with vision occluded (Kim et al., 2008), which exhibit significantly elevated α-values compared to when vision is left available. This high level of baseline constraint suggests that occluding vision impacts both the open- and closed loop control of posture, which is in agreement with our control model (Figure 8.1). However, a lack of difference in the MSE analysis, which occurs at time scales less than 210 ms, indicates a uniform open-loop state. Therefore, we conclude that the observed changes in the control of quiet upright standing in response to a stepwise cooling of the feet occur at longer time scales and are indicative of a change in the closed-loop, feedback-based control of posture. This interpretation is in agreement with the model proposed by Collins & DeLuca (1993), who identified that limiting vision may serve to stiffen the musculoskeletal system, which in turn will constrain the COP fluctuations. As we observe a uniform open-loop state, further experimentation, with vision left intact, is needed to identify if cooling the skin of the feet impacts both the short and long time scale fluctuations of posture.

8.5 Stochastic Resonance Improves the Perception of Body Position

The final study of this dissertation explored if stochastic resonance was able to improve the perception and control of posture when the skin was cooled to levels that elicit increases in cutaneous sensory thresholds similar to those seen in clinical populations, such as individuals with MS. SR is thought to improve the control of posture through enhancing the ability to detect external information. The application of SR to the soles of the feet improved the ability to perceive body position, as identified by a reduction in the error of a postural repositioning task. Such that the more sensation was knocked down through cooling of the skin, the more SR was able to improve the perception of posture. The results of this study build on the growing evidence that SR is able to improve posture (Priplata et al., 2002), and indicate that SR may be able to confer benefits across a range of sensory conditions, with potentially greater benefits under more impaired sensory function, as shown in the current study. This position is supported by the work of Stephen et al. (2012) who also reported that SR improved stride parameters more among individuals with the greatest levels of impairment.

We did not observe the expected changes in the control of quiet standing when SR was applied to the soles of the feet. It is likely that the high amount of constraint placed on the postural control system due to the occlusion of vision, and indicated by scaling exponent values near 1.5, may obscure our ability to observe the effects of SR.

8.6 Conclusions and Future Directions

The results of this dissertation suggest that changes in the loads on the plantar surface of the feet associated with changes in posture influence the detection of vibrations

applied to the plantar surface of the feet. Furthermore, we show that cooling the skin of healthy individuals can mimic a reduced ability to identify external information with the feet, as seen in clinical populations such as individuals with MS. While cooling the skin exhibited subtle changes in the control of upright standing, the nature of the findings suggests that reducing the temperature of the skin, which results in elevated cutaneous sensory thresholds, impacts the closed-loop control of posture, which relies on feedback and occurs on long time scales. Finally, we demonstrated that shoes that are able to apply SR to the soles of the feet are an aid that can improve the perception of body orientation.

Apart from the aforementioned need to experimentally validate the claims made here regarding the occlusion of vision, it is quite clear that we need to move toward an understanding of how pressure fluctuations under the feet influence the detection of environmental information. Heretofore, the research in postural dynamics has focused on measures that can tease out differences between clinical and non-clinical states. The results of the studies presented here support Gibson's theory of ecological perception—the notion that individuals "move to perceive and perceive to move" (Gibson, 1962)—in that changes in the weighting of the feet brought about by shifting posture may alter the ability to detect external vibrations. Future work is needed to determine if pressure fluctuations that occur under the feet are sufficient to alter the ability to detect environmental information. The evidence presented here suggests that individuals with cutaneous sensory loss may modulate postural and locomotor behavior in order to maintain access to environmental information, suggesting a strong duality in the optimization criteria used in the control of posture: one relates to stability and another to accessing perceptual information. This postulate is supported by the work of Riccio and

colleagues who suggest that changes in postural dynamics arise out of an effort to maintain environmental awareness (Riccio, 1993; Riccio et al., 1992; Riccio & Stoffregen, 1991; van Emmerik & van Wegen, 2000). The studies of this dissertation identify a pathway by which altering postural fluctuations may lead to alterations in the ability to detect external information. Identifying whether changes in postural fluctuations arise in individuals with clinical disorders (e.g., multiple sclerosis and diabetes) in order to improve or maintain the ability to detect external information will provide further context for understanding the changes in posture that accompany disease.

The results of the studies presented here indicate that large changes in the forces under the feet bring about alter the ability to detect external vibration. However, the temporal aspect of the shifts in plantar pressure remain unclear, and identifying this in the future will allow for further contextualization of changes in postural variability. The trend for difference in the sensory thresholds of the forefoot suggest that small changes in the weighting of the forefoot (~5% body weight) may be sufficient to alter the ability to detect external information. Future experimentation is needed to identify if the pressure fluctuations that occur under the feet are sufficient to alter the detection of external information. Developing experiments that elucidate if fluctuations in plantar pressure impact the detection of external information will enhance our understanding of whether individuals alter their plantar pressures in order to facilitate information detection. These insights will allow for contextualization of the way in which individuals with clinical sensory loss re-optimize postural fluctuations in order to meet two apparent goals: stabilize posture and pick up environmental information.

8.7 References

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APPENDICES

APPENDIX A

INFORMED CONSENT DOCUMENTS: STUDY 1

Consent Form for Participation in a Research Study
University of Massachusetts Amherst

Researcher(s):	Stephanie L. Jones, PhD, Mike Busa, MS, Richard E.A. Van Emmerik, PhD
Study Title:	Improving Cutaneous Sensation and Balance in People with Multiple Sclerosis
Funding Agency:	National Multiple Sclerosis Society

1. WHAT IS THIS FORM?

This form is called a Consent Form. It will give you information about the study so you can make an informed decision about participation in this research. It will also describe what you will need to do to participate and any known risks, inconveniences or discomforts that you may have while participating. We encourage you to take some time to think this over and ask questions now and at any other time. If you decide to participate, you will be asked to sign this form and you will be given a copy for your records.

2. WHO IS ELIGIBLE TO PARTICIPATE?

We are recruiting two groups of participants for a total of 40 individuals. One group will include 20 people who have been diagnosed with Multiple Sclerosis (MS) (for at least 6 months) and have mild to moderate balance problems (require no use or minimal use of walking aids). The second group will include 20 healthy individuals who do not have MS. Both groups will include males and females between the ages of 21 and 65 and will not have any non-MS neurological, musculoskeletal, metabolic, cardiovascular or other major diseases or injuries.

3. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to test the effectiveness of enhancing sensation of the bottom of the feet to improve balance in people with MS. In this study we will use small vibrating devices in the insoles of shoes to enhance the skin's sensation and we will use data from a force measuring platform and special cameras that see reflective markers to determine whether balance is improved because of these devices. The results from this study will allow clinicians and researchers to gain a better understanding of how skin sensation aids in balance control for people with MS. The information that will be obtained will test the effectiveness of vibrating devices in the shoes to improve balance that could be used as an aid to assist those with MS who have balance problems.

4. WHERE WILL THE STUDY TAKE PLACE AND HOW LONG WILL IT LAST?

The study will be conducted in the Motor Control Laboratory (Totman Building), in the Department of Kinesiology at the University of Massachusetts Amherst. This study is expected to last for 18 months. If you participate you will take part in a single testing session that will last for approximately 3 hours.

5. WHAT WILL I BE ASKED TO DO?

If you agree to take part in this study, you will be asked to do the following:

At your visit you will be asked to fill out questionnaires about your fatigue, health status, MS symptoms (if applicable) and balance confidence. You may skip any question you feel uncomfortable answering. Your walking ability will be tested (25 feet at normal and brisk paces) as will your walking balance (walking 16.4 feet while kicking small objects to the side). You will also be asked to perform foot tapping tests (while seated) and a task of rising from a chair repeatedly. Your skin sensitivity will be tested using small threads and devices that provide light vibrations to the soles of your feet, while you are 1) lying down and 2) standing a mat that measures the pressure under your feet.

Part 2: You will be asked to perform several standing balance tasks (standing, leaning, heel to toe stance) while wearing shoes that have vibrating devices set into the insoles. During these tests you will wear small reflective markers taped to your skin that will be recorded using high speed cameras that can very accurately track your movements. You will be asked to perform these tests before vibrations are applied to your feet, while vibrations are applied to your feet, and after vibrations have been removed from your feet.

The total time for testing will be approximately 3 hours during which you will be provided with adequate rest to minimize fatigue.

6. WHAT ARE MY BENEFITS OF BEING IN THIS STUDY?

You will not experience any lasting benefits from participating in this study; however, you may experience a temporary improvement in your skin sensation and balance performance during the testing session, while vibration is applied to your feet. Your participation in this study will aid our understanding of the role of skin sensitivity in balance control of those with MS and may provide evidence to support the use of sensory enhancement as an aid to improve balance in people with MS.

7. WHAT ARE MY RISKS OF BEING IN THIS STUDY?

We believe that the risks involved in this project are no different than what you encounter as you move about your environment in your normal daily life. Although we allow sufficient rest throughout the protocol to prevent you from becoming tired, you may experience some physical or mental fatigue during or following the protocol because you will be asked to stand and perform balance tasks. A chair will be provided for you to rest should you choose.

8. HOW WILL MY PERSONAL INFORMATION BE PROTECTED?

The following procedures will be used to protect the confidentiality of your study records. The researchers will keep all study records, including any numeric codes to your data, in a secure location within a locked cabinet, in a locked laboratory. Research records will be labeled with an unidentifiable code. A master key that links names and codes will be maintained in this secure location. No electronic records containing identifiable information will be generated. Electronic records of unidentified data will be stored and analyzed on password-protected computers. Only the members of the research staff will have access to the passwords. At the conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations.

9. WILL I RECEIVE ANY PAYMENT FOR TAKING PART IN THE STUDY?

By participating in this study you will receive a participant stipend of $25 to cover transportation costs. This payment will not be made if you fail to appear in the Motor Control Laboratory for your testing session.

10. WHAT IF I HAVE QUESTIONS?

Take as long as you like before you make a decision. We will be happy to answer any question you have about this study. If you have further questions about this project or if you have a research-related problem, you may contact the researcher(s), Stephanie Jones (413-545-4959; email: sljones@kin.umass.edu), Mike Busa (413-545-1332; mbusa@kin.umass.edu) or Richard Van Emmerik (413-545-0325; email:

rvanemmerik@kin.umass.edu). If you have any questions concerning your rights as a research subject, you may contact the University of Massachusetts Amherst Human Research Protection Office (HRPO) at (413) 545-3428 or humansubjects@ora.umass.edu.

11. CAN I STOP BEING IN THE STUDY?

You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. There are no penalties or consequences of any kind if you decide that you do not want to participate.

12. WHAT IF I AM INJURED?

The University of Massachusetts does not have a program for compensating subjects for injury or complications related to human subjects research, but the study personnel will assist you in getting treatment.

13. SUBJECT STATEMENT OF VOLUNTARY CONSENT

When signing this form I am agreeing to voluntarily enter this study. I have had a chance to read this consent form, and it was explained to me in a language which I use and understand. I have had the opportunity to ask questions and have received satisfactory answers. I understand that I can withdraw at any time. A copy of this signed Informed Consent Form has been given to me.

______________________	__________________	_________
Participant Signature:	Print Name:	Date:

By signing below I indicate that the participant has read and, to the best of my knowledge, understands the details contained in this document and has been given a copy.

______________________	__________________	_________
Signature of Person Obtaining Consent	Print Name:	Date:

APPENDIX B

INFORMED CONSENT DOCUMENTS: STUDIES 2 & 3

Consent Form for Participation in a Research Study
University of Massachusetts Amherst

Researcher(s):	Michael Busa, MS, Stephanie Jones, PhD, Brian Umberger PhD, Richard Van Emmerik, PhD
Study Title:	Plantar Pressure, Cutaneous Sensation and Stochastic Resonance: An Examination of Factors Influencing the Control and Perception of Posture
Funding Agency:	none

1. WHAT IS THIS FORM?

This form is called a Consent Form. It will give you information about the study so you can make an informed decision about participation in this research. It will also describe what you will need to do to participate and any known risks, inconveniences or discomforts that you may have while participating. We encourage you to take some time to think this over and ask questions now and at any other time. If you decide to participate, you will be asked to sign this form and you will be given a copy for your records.

2. WHO IS ELIGIBLE TO PARTICIPATE?

We are recruiting 12 individuals to participate in this study. All participants will be free of neurological musculoskeletal, metabolic, cardiovascular or other major diseases or injuries. The group will consist of female participants between the ages of 18 and 40 years.

3. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to test the role that impaired sensation has on control of upright standing. In this study we will use small vibrating devices in the insoles of shoes to 1) test how reduced sensation, through cooling of the skin, influences the ability to control and perceive standing posture, and 2) test if enhancing the skin's sensation through undetectable vibrations can improve the control of posture when the skin is cooled. To accomplish this we will use data from a force measuring platform and special cameras that see reflective markers placed on your body to determine balance performance. The results from this study

will allow clinicians and researchers to gain a better understanding of how skin sensation influences balance control. The information that will be obtained will test the effectiveness of vibrating devices in the shoes to improve balance when sensory function is reduced.

4. WHERE WILL THE STUDY TAKE PLACE AND HOW LONG WILL IT LAST?

The study will be conducted in the Biomechanics Laboratory (Totman Building), in the Department of Kinesiology at the University of Massachusetts Amherst. This study is expected to last for 18 months. If you participate you will take part in one testing session that will last for approximately 2 hours.

5. WHAT WILL I BE ASKED TO DO?

If you agree to take part in this study, you will be asked to do the following:

You will have your height, weight, foot length and foot width measured. You will then have your skin sensitivity tested using a device that provides light vibrations to the soles of your feet and while wearing a special shoe that has small vibrating discs fit into the sole. This testing will be performed in two ways: 1) while you are lying down and 2) while you are standing. These procedures will be repeated at four skin temperatures (normal body temperature and 7, 14 and 21 degrees Fahrenheit below that temperature), where placing them on ice, for approximately 2 minutes at a time, will cool your feet. The coldest your skin temperature will get is approximately 50 degrees Fahrenheit, a temperature, which is significantly above that which causes frostbite. The temperature of your skin is related to the ambient temperature, such that in a room of 73 degrees Fahrenheit the skin temperature will be 77 degrees Fahrenheit. The room in which the testing will take place will create ambient conditions as a starting point; your feet will then be cooled in the manner described above. You will then be asked to perform a series of postural tasks, such as standing quietly as well as recreating a postural configuration. Each of these tasks will be performed twice. In one of these two tests undetectable vibrations will be applied to the soles of your feet. While performing these tests you will wear small reflective markers taped to your skin that will be recorded using high speed cameras that can very accurately track your movements. These cameras record only the motion of the reflective markers; no identifiable video images will be recorded.

The total time for testing for the testing session will be approximately 2 hours, and you will be provided with adequate rest to minimize fatigue.

6. WHAT ARE MY BENEFITS FROM BEING IN THIS STUDY?

You will not experience any lasting benefits from participating in this study; however, you may experience a temporary improvement in your skin sensation and balance performance following the second testing session where vibrations are applied to your feet. Your participation in this study will further our understanding of the role of skin sensitivity on the control of balance, as well as the role undetectable vibrations can play in improving standing posture in those people who experience balance problems.

7. WHAT ARE MY RISKS FROM BEING IN THIS STUDY?

We believe that the risks involved in this project are minimal, and may include slight numbness of the feet as a result of the cooling, which should stop shortly after testing is complete. Although we allow sufficient rest throughout the protocol to prevent you from becoming tired, you may experience some physical or mental fatigue during or following the protocol because you will be asked to stand and perform balance tasks. A chair will be provided for you to rest should you choose.

8. HOW WILL MY PERSONAL INFORMATION BE PROTECTED?

The following procedures will be used to protect the confidentiality of your study records. The researchers will keep all study records, including any numeric codes to your data, in a secure location within a locked cabinet, in a locked laboratory. Research records will be labeled with an unidentifiable code. A master key that links names and codes will be maintained in the same locked cabinet and locked laboratory as the other data. No electronic records containing identifiable information will be generated. Electronic records of unidentified data will be stored and analyzed on password-protected computers. Only the members of the research staff will have access to the passwords. At the conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations.

9. WILL I RECEIVE ANY PAYMENT FOR TAKING PART IN THE STUDY?

There will be no compensation for participating in this study.

10. WHAT IF I HAVE QUESTIONS?

Take as long as you like before you make a decision. We will be happy to answer any question you have about this study. If you have further questions about this project or if you have a research-related problem, you may contact the researcher(s), Mike Busa (413-545-1332; mbusa@kin.umass.edu) or Richard Van Emmerik (413-545-0325; email: rvanemmerik@kin.umass.edu). If you have any questions concerning your rights as a

research subject, you may contact the University of Massachusetts Amherst Human Research Protection Office (HRPO) at (413) 545-3428 or humansubjects@ora.umass.edu.

11. CAN I STOP BEING IN THE STUDY?

You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. There are no penalties or consequences of any kind if you decide that you do not want to participate.

12. WHAT IF I AM INJURED?

The University of Massachusetts does not have a program for compensating subjects for injury or complications related to human subjects research, but the study personnel will assist you in getting treatment in the unlikely event that you are injured during the testing.

13. SUBJECT STATEMENT OF VOLUNTARY CONSENT

When signing this form I am agreeing to voluntarily enter this study. I have had a chance to read this consent form, and it was explained to me in a language which I use and understand. I have had the opportunity to ask questions and have received satisfactory answers. I understand that I can withdraw at any time. A copy of this signed Informed Consent Form has been given to me.

____________________	____________________	__________
Participant Signature:	Print Name:	Date:

By signing below I indicate that the participant has read and, to the best of my knowledge, understands the details contained in this document and has been given a copy.

____________________	____________________	__________
Signature of Person Obtaining Consent	Print Name:	Date:

APPENDIX C:

THE RELATIONSHIP BETWEEN SENSORY THRESHOLDS MEASURED BY C-2 TACTORS AND BIOTHESIOMETER.

The purpose of this investigation was to assess the relationship between the C-2 tactors and the biothesiometer. This was done in conjunction with the data collection of the first study. In this comparison we identified the minimum detectible stimulus, or sensory threshold, each subject could identify under both the fore- and rearfeet while in the supine position. The sensory threshold with the biothesiometer was determined when participants identified the onset of vibration as the oscillation (120 Hz) amplitude of the Biothesiometer probe was gradually increased. During quiet standing, sensory function was assessed by C-2 tactors embedded in the soles of custom modified sandals (Teva, Deckers Outdoor Corporation, Goleta, CA), using a 4:2:1 technique (Chong & Cros 2004). In the 4:2:1 method for determining sensory threshold, the 30-350 Hz (white noise) signal amplitude was increased from the lowest level four levels at a time until the participant was able to detect it. The signal was then decreased two levels at a time until the participant was unable to detect it. Finally, the signal was modulated one level at a time until neighboring vibrations produced responses where one was identifiable and the other was not. With both devices, sensory threshold was identified as the lowest voltage at which participants could detect the vibration.

The thresholds from the left and right feet were averaged, as there was no difference between the left and right feet. The thresholds, quantified with each device were then used to compute a Pearson-product moment correlation. The devices revealed a

significant relationship between the two devices (r=0.449, p=0.028). The strength of this relationship was lower than we had originally expected. However this is likely due to how course grained the steps in tactor voltage was. It is possible (likely) that if the steps between tactor amplitude levels were smaller we may see a stronger relationship between the two devices.

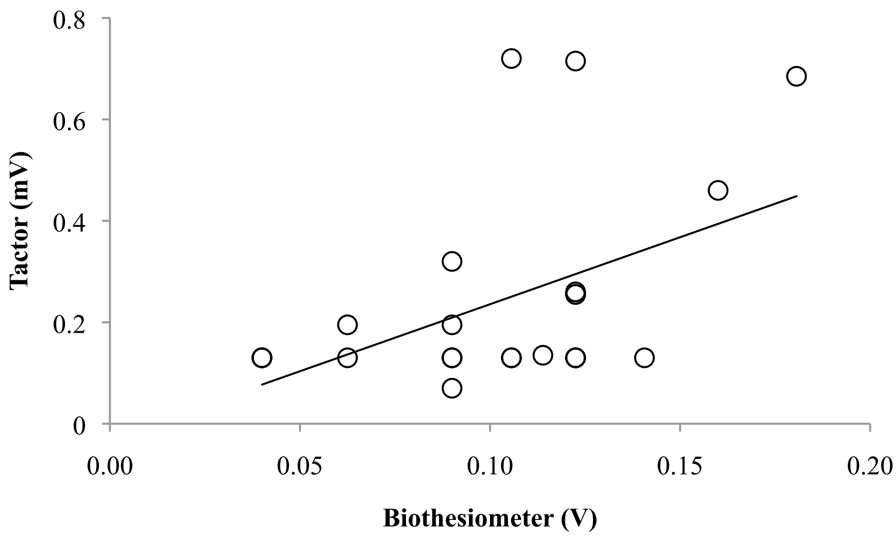

Figure C.1: Comparison of Biothesiometer and Tactors. Points indicate individual subject values for cutaneous sensory threshold measurements in the supine position measured by both biothesiometer and tactors. Line is indicative of linear regression fit r^2=0.20.

APPENDIX D

ORDER OF TRIALS IN STUDY 2 & 3

In studies 2 and 3 we examined both the control of quiet standing and the ability to recreate body positions. Figure D.1 identifies the trials in which SR was and was not applied to the feet. The sequentially numbered column identifies the trial order. The ✓ marks indicate the trials where the SR was applied.

		Subject											
		1	2	3	4	5	6	7	8	9	10	11	12
Baseline	1					✓	✓	✓	✓	✓	✓		
	2					✓	✓	✓	✓	✓	✓		
	3					✓	✓	✓	✓	✓	✓		
	4	✓	✓	✓	✓							✓	✓
	5	✓	✓	✓	✓							✓	✓
	6	✓	✓	✓	✓							✓	✓
Baseline-5	7						✓				✓		✓
	8						✓				✓		✓
	9						✓				✓		✓
	10	✓	✓	✓	✓	✓		✓	✓	✓		✓	
	11	✓	✓	✓	✓	✓		✓	✓	✓		✓	
	12	✓	✓	✓	✓	✓		✓	✓	✓		✓	
Baseline-9	13	✓		✓	✓	✓				✓		✓	
	14	✓		✓	✓	✓				✓		✓	
	15	✓		✓	✓	✓				✓		✓	
	16		✓				✓	✓	✓		✓		✓
	17		✓				✓	✓	✓		✓		✓
	18		✓				✓	✓	✓		✓		✓
Baseline-14	19				✓	✓		✓		✓	✓		✓
	20				✓	✓		✓		✓	✓		✓
	21				✓	✓		✓		✓	✓		✓
	22	✓	✓	✓			✓		✓			✓	
	23	✓	✓	✓			✓		✓			✓	
	24	✓	✓	✓			✓		✓			✓	

Figure D.1: Order of Trials with and without SR for Study 3. ✓indicate trials where SR was applied. Labels indicate the temperature condition.

APPENDIX E

RESULTS OF SKIN COOLING PILOT WORK

The results of pilot testing (n=3) indicated that cooling the feet caused significant increase in the sensory threshold in both portions of the feet. These changes in skin temperature were brought about by checking the cooling of the feet for 30 s at a time. The time for each measurement was 120 s for all time points. Pilot work was guided by the work of Remelius et al. (2012), who observed that individuals with MS exhibit a 100% increase in sensory thresholds compared to individuals without MS.

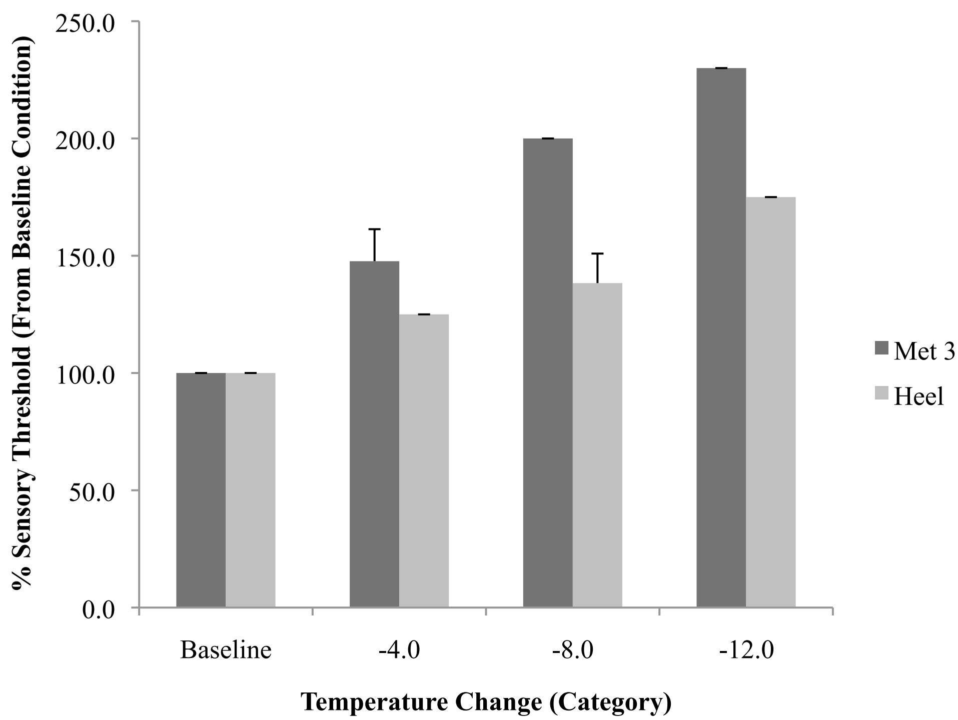

Figure E.1: Impact of Temperature on Sensory Threshold. Percent increase in the sensory thresholds as a result of decreasing skin temperature based on n=3, bars indicate mean + SD.

Furthermore, we piloted the rate at which the temperature of the skin warmed after 2 minutes of cooling. The skin temperature was maintained (~1°C) for

approximately 120 s after the feet were taken off ice. This suggests that skin temperature should be checked at least every 60 seconds and feet should not remain off of ice for more than 120s. Based on these results once a skin temperature, below baseline, was established participants had their skin temperature checked every 60 s and were never off of the ice for more than 120 s. This was to ensure that individuals skin temperature never warmed more than 1°C once a skin temperature was established.

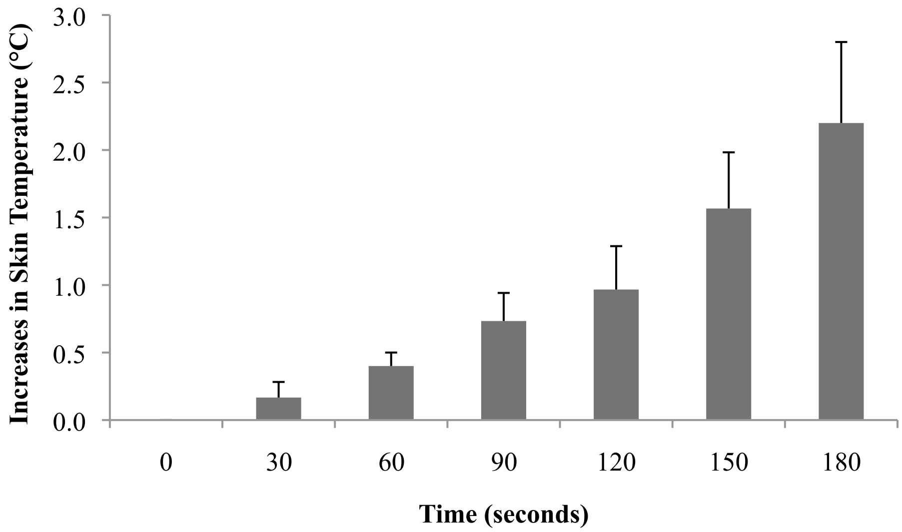

Figure E.2: Warming of the Feet in Response to Cooling the Feet by 4°C. Bars are indicative of mean (n=3) + SD.

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