PLANTAR OR PALMAR TACTILE AUGMENTATION IMPROVES LATERAL POSTURAL BALANCE WITH SIGNIFICANT INFLUENCE FROM COGNITIVE LOAD

A Thesis

by

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ABSTRACT

Peripheral neuropathy of the lower legs is a serious nervous system disorder that increases the risk of falls due to decreased sensation on the plantar surface of the feet. Although it seems intuitive to address this issue at the location of reduced sensation, many current rehabilitation approaches target other locations of the body (i.e., sensory compensation). The efficacy of these methods can be limited due to the heavy cognitive load needed to interpret the compensatory cues. The objective of this study is to test our hypothesis that tactile augmentation on the plantar surface is more effective than indirect compensatory sensory feedback at improving postural regulation when plantar cutaneous feedback is reduced.

In our experiments, six healthy human subjects stood on a lateral balance board and maintained their balance for as long as possible until the balance board contacted the ground for a fixed number of trials. During these experiments, subjects were instructed to close their eyes to remove visual feedback and increase dependency on tactile feedback for balancing. They also had a layer of foam placed between their feet and the balance board to simulate the effect of reduced tactile feedback from the foot sole. The effects of tactile augmentation on the foot sole or the palm were tested by applying transcutaneous electrical stimulation on the calcaneal or ulnar nerve during the balance tests with and without a cognitive task. The results from the experiment indicate that tactile augmentation at either the foot or the hand was effective at improving balance when no cognitive demand was present. However, when the cognitive task was given to subjects during the experiments, the balance time was further increased for plantar cutaneous augmentation but decreased back to the original level for

palmar cutaneous augmentation. This result suggests that the location of sensory augmentation is important especially when cognitive capacity is limited.

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CONTRIBUTORS AND FUNDING SOURCES

Contributors

This work was supervised by a thesis advisory committee consisting of Professor Hangue Park [advisor], Professor Steven Wright, and Professor Jun Kameoka of the Department of Electrical Engineering, Professor Roozbeh Jafari of the Department of Biomedical Engineering, and Professor Shuo-Hsiu Chang of the UT Health Science Center at Houston.

All other work conducted for the thesis was completed by Jacob Azbell, with contributions from Jaekwan Park of the Kinesiology Department and Angie Cisneros and Abhimanyu Arora of the Electrical Engineering Department.

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CHAPTER I INTRODUCTION

In the US alone, falls result in more than 2.8 million injuries treated in emergency departments annually, including over 800,000 hospitalizations and more than 27,000 deaths [1]. Many of these falls are caused by balance deficit, which is the diminished ability to self-regulate balance. Aside from falls, balance deficit may also result in asymmetric loading of intact musculoskeletal structures during walking and may be followed by undesirable compensation by the body to maintain balance and stability, which often leads to secondary complications, such as osteoarthritis and lower back pain. Furthermore, balance deficit can signal the beginning of a decline in function and independence because it can limit the amount of exercise an individual is able to partake in, which cascades into further health issues. One disorder that leads to a balance deficit is peripheral neuropathy (PN), which is a condition in which periphery sensorimotor neurons are damaged or diseased such that their ability to transmit signals to and from the brain is limited. PN can be caused by a number of issues, such as aging, diabetes, chemotherapy, hereditary disorders, inflammatory infections, autoimmune diseases, protein abnormalities, exposure to toxic chemicals, poor nutrition, kidney failure, chronic alcoholism, and certain medications – especially those used to treat cancer and HIV/AIDS [2]. PN can result in seriously diminished sensory feedback on the plantar surface of the foot, and this sensory loss can make detrimental changes in postural balance regulation, even in simple routine tasks, such as walking or standing [3-5]. This deficit in postural balance regulation makes PN a large contributor to the number of dangerous falls that occur every day. Thus, decreased plantar cutaneous feedback due to peripheral neuropathy is a serious issue that needs to be addressed to ensure the safety and quality of life for those affected by it.

In addressing the balance deficit caused by decreased plantar cutaneous feedback, several compensatory approaches have been introduced. These compensatory approaches provide indirect sensory cues instead of directly addressing the sensory deficit at the plantar surface. For example, Sihvonen and colleagues demonstrated that balance training with a computerized force platform and a visual feedback screen could improve the balance of elderly women [6]. Visual feedback is generally accepted as a compensatory sensory modality for individuals who have a deficit in sensory feedback from the foot or vestibular system, and it was used as such in this case. As another example, Wall and colleagues proved that vibrotactile feedback applied to the sides of the trunk or shoulders could be used to reduce head-tilt angle and center of pressure displacements during standing posture [7]. As a similar approach, vibrotactor arrays placed around the waist could reduce anterior-posterior trunk tilt during quiet standing in individuals with vestibular deficits [8], [9]. The underlying principle of these indirect approaches on improving poor balance is that compensatory feedback can be interpreted in the central nervous system in order to adjust and control motor output to improve balance. However, the efficacy of these indirect approaches can be limited due to their reliance on an associated cognitive load, which may decrease consistency of motor output and increase response time and fatigue [10], [11]. This notion is depicted in Fig. 1. As seen in the figure, the indirect pathway of compensatory approaches more heavily relies on pre-frontal cortical processing than the original sensory pathway for balance control through plantar cutaneous feedback. The sensory feedback pathway for plantar cutaneous feedback can be completely independent of the pre-frontal cortex. Thus, compensatory approaches may not be the ideal method of improving balance for those who suffer from PN.

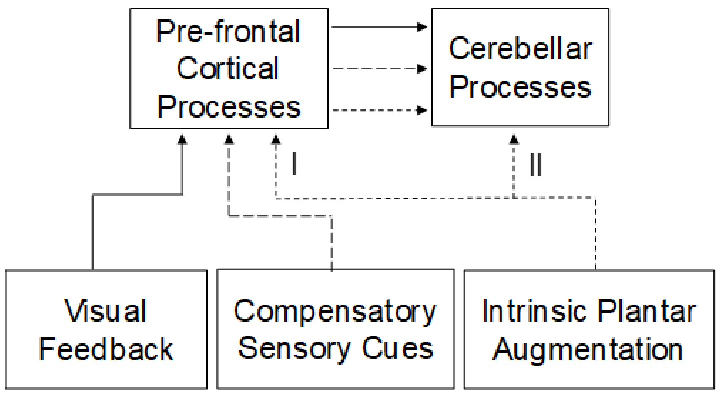


Figure 1: Sensory Feedback Pathways for Intrinsic and Compensatory Balance Cues

Several mechanisms of feedback influence postural regulation. Visual feedback and compensatory sensory cues (i.e., sensory feedback unassociated with balancing) are interpreted in the pre-frontal cortex, which relies on cognition to plan and execute movements, before being delivered to the cerebellum. However, augmented plantar cutaneous feedback can be delivered directly to the cerebellum (II), bypassing the pre-frontal cortex (I). Due to this discrepancy, plantar cutaneous augmentation should prove to be less dependent on cognitive processing than visual or compensatory sensory augmentation in regards to postural regulation.

Augmenting plantar cutaneous feedback as a direct approach to address the decreased plantar cutaneous feedback would minimize the issue of the cognitive involvement that plagues compensatory approaches. Additionally, there is a general consensus that plantar cutaneous feedback plays an important role in balance regulation, especially in a challenging environment. Human and animal experiments have shown that plantar cutaneous feedback is critical for recovery of balance after postural perturbations during locomotion [12],[13] and becomes even more crucial in maintaining balance if the locomotor behavior is challenging [14],[15]. Considering that postural regulation is a challenging task for individuals with reduced plantar cutaneous feedback, tactile augmentation on the foot sole and its effects on balance need to be thoroughly investigated.

A pair of related studies showed that electrical stimulation applied on the plantar area could improve the balance of people with diabetic neuropathy, potentially by increasing the sensitivity of plantar cutaneous receptors [16], [17]. In another study, vibrating insoles could enhance balance for elderly subjects and subjects with diabetic neuropathy, which was interpreted as white noise enhancing sensorimotor function by stochastic resonance [18], [19]. Although the plantar sensation was modulated, these prior studies did not augment plantar cutaneous feedback, because the stimulation or vibration was not timed with the original plantar sensation. To augment plantar cutaneous feedback and directly compensate for the decreased plantar cutaneous feedback, closed-loop operation is important. In other words, plantar cutaneous augmentation should be applied based on the lateral sway of the body or the pressure on the foot, to be timed with the original plantar sensation.

Another aspect to consider is that direct intervention onto the foot sole would not be effective for elderly people or diabetic neuropathy patients because they have often lost sensitivity of the plantar nerves. Furthermore, direct intervention onto the foot sole can provide discomfort to the user. Instead, we can augment plantar cutaneous feedback by stimulating the distal-tibial nerve and its branches, which can be accessed at the caudal aspect of the medial malleolus and are located close to the skin [20], [21]. The distal-tibial nerve is innervated onto the foot sole and is mainly composed of cutaneous axons. It is highly likely that the transcutaneous electrical stimulation, applied onto the skin along the path of the distal-tibial nerve, can selectively elicit plantar cutaneous feedback [22], [23]. Therefore, transcutaneous distal-tibial nerve stimulation is a promising approach for tactile augmentation from the foot sole and could allow for improvement in postural regulation for individuals with reduced plantar sensation.

In this thesis, we present a novel closed-loop transcutaneous distal-tibial nerve stimulation methodology as an approach to direct plantar cutaneous augmentation. The overall research goal of this study is to determine the efficacy of closed-loop transcutaneous distal-tibial nerve stimulation on improving postural regulation in people with compromised plantar cutaneous feedback [24], [25]. We hypothesize that the closed-loop plantar cutaneous augmentation, based on the lateral sway of the body, will improve lateral balance for people standing in a challenging condition for balance. We also hypothesize that closed-loop plantar cutaneous augmentation will be more effective at improving balance than providing compensatory sensory cues, such as palmar cutaneous augmentation. The reasoning behind this hypothesis is that plantar cutaneous feedback is intrinsically associated with sway and postural balance, while palmar cutaneous feedback provides only an auxiliary sensory cue in regards to balance [26]. Additionally, we hypothesize that a challenging cognitive task will be detrimental to the efficacy of palmar augmentation but will not affect the efficacy of plantar augmentation. This is because compensatory cues, such as palmar augmentation, are mainly processed by the prefrontal cortex, while intrinsic sensory cues for balance, such as plantar augmentation, are mainly processed by the cerebellum. A cognitive task will not diminish the ability to interpret plantar sensory augmentation because these intrinsic balance cues are processed by the balance center (i.e., cerebellum) operating with minimal cognitive involvement.

CHAPTER II METHODS

Human Subject Recruitment

The experiments in this study were performed in accordance with relevant guidelines and regulations, according to the procedure described in the protocol approved by the Institutional Review Board of Texas A&M University (IRB2018-1511F). Informed consent was collected from all subjects. Six healthy human subjects with no history of neurological disorders participated in the experiments in this study. The subject group consisted of one female and five males. All subjects were over the age of 18, and the mean age of subject group was 25.

Lateral Balance Board and Handrail

To measure the lateral balance in a challenging environment, the lateral balance board (3B Scientific W15075 Eucalyptus Wood Lateral Balance Rocker Board) was located on the ground with a stationary handrail affixed to the ground in front of the balance board. During the experiments, data was collected to measure the time duration that subjects could remain balanced on the balance board (i.e., balance time). This duration was defined as the time between the subject releasing the handrail and the moment that either side of the balance board contacted the ground. In order to record this time duration, custom-made force sensors were placed on the handles of the handrail and on the bottom edges of the balance board to detect both the release of a subject's hand from the handrail and the contact between the balance board and the ground.

Optical Motion Capture System

The movement of the lateral balance board was recorded by an OptiTrack motion capture system (NaturalPoint, Inc., OR, USA). The system consists of 8 equally-spaced infrared cameras and user-placed optical markers by which the cameras can detect and track movement. The balance board had optical markers placed on each side so that the motion capture system could track the movement of the balance board during experiments. From this data, the effect of tactile augmentation on postural regulation could be quantified, in addition to the balance time [27].

Closed-loop Tactile Augmentation System

To augment the tactile feedback from the foot sole or the palm, we designed a system that operates as a real-time closed-loop monitoring and stimulation system. First, we measured the distance between each side of the balance board and the ground using an ultrasonic distance sensor (HC-SR04) with a distance monitoring range from 2 to 400 cm. The distance sensor was placed on the left end of the lateral balance board (from the subject's perspective) facing downwards towards the ground. The sensor measured 3 cm when the board was touching the ground on the left side (where the sensor is located), and 14 cm when the board was touching the ground on the right side. The board was evenly balanced when the sensor measured 8.5 cm.

The distance data from the sensor was delivered to an Arduino Nano microcontroller, which then sent a signal to a stimulator to provide electrical stimulus to subjects. The stimulation was provided only after a subject was deemed off balance by the system. This occurred when either side of balance board more than 1.5 cm vertically below the perfectly balanced position. The electrical stimulus was applied to either the calcaneal nerve or ulnar nerve to augment the plantar or palmar cutaneous feedback, respectively [25]. Stimulation was provided to the foot sole or the palm on the leaned side of the subject. As a result, a larger tactile sensation was evoked on the side that is closer to the ground (i.e., the side that the subject is leaning towards). Since the balance board is not a familiar environment for subjects, we expect that the stronger tactile feedback on the foot of the leaned side would be intuitive for subjects to interpret as a balancing cue. This is expected because the foot on the leaned side experiences stronger tactile feedback in normal situations. Stimulation was turned off when the board was balanced, with a hysteresis of ±1.5 cm (when the sensor output was between 7 and 10 cm).

The stimulator circuit consisted of an H-bridge to produce biphasic stimulus from the control signal given by the microcontroller, which is level shifted to the desired stimulation voltage before reaching the H-bridge. Each H-bridge in the stimulator circuit consists of a CD4007 CMOS transistors (Texas Instruments, TX, USA), and each level shifter consists of two 2N3904 transistors. The biphasic stimulation was provided at 100 Hz with 1-ms pulse width (i.e., 20% duty factor), and the stimulation voltage amplitude was adjusted for each subject to attain appropriate sensation on the desired area of the body. The maximum stimulation current was limited to 20 mA. The output of the stimulator was transmitted to gel electrode pairs (Patients Choice® Silver 0.8" Round Tan Tricot Electrode), which were placed on the subjects' skin along the calcaneal nerve or the ulnar nerve that innervates onto the foot sole or the palm, respectively. A diagram of the entire experimental system is shown in Fig. 2, and a depiction of the biphasic stimulation is pictured in Fig. 3. The Arduino code that controlled the timing of stimulation based on the proximity sensor feedback is included in Appendix A.

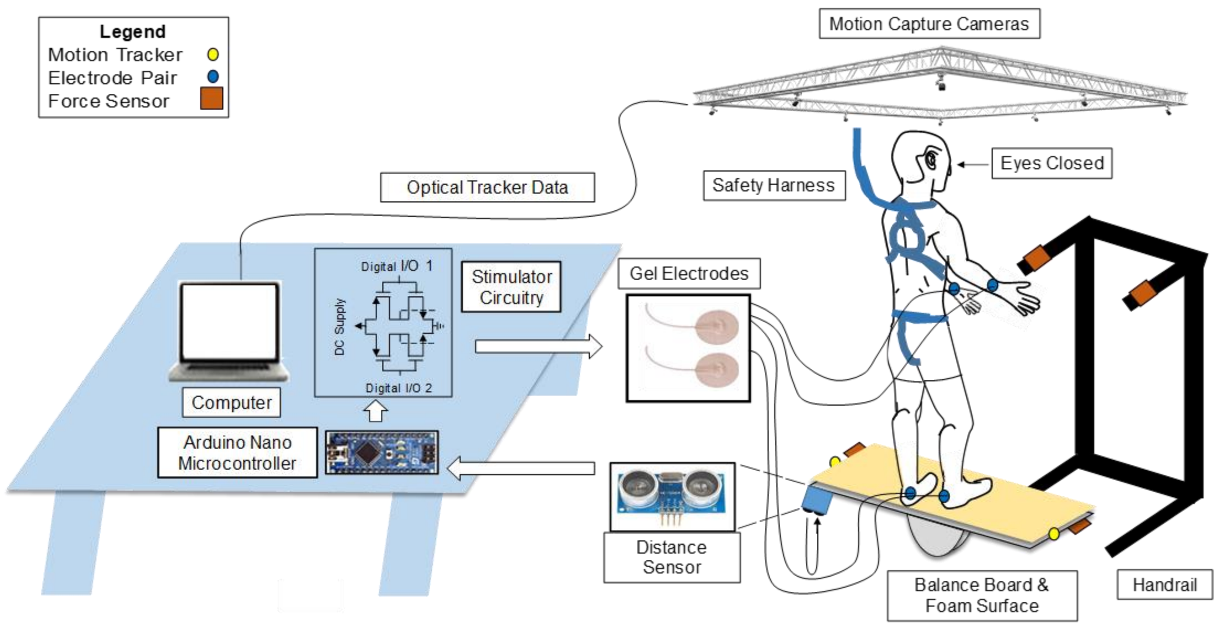


Figure 2: Diagram of Experimental System

This diagram depicts the lateral balance board, closed-loop transcutaneous electrical stimulation, and motion capture system. In the system, each subject obtained a balanced position with the help of the handrail. Once balance was achieved, the subject closed his or her eyes and released the handrail. In the experiment, the subject received plantar or palmar cutaneous augmentation of the side they were leaning towards. The system carries this out by utilizing a distance sensor that relays the balance board's distance from the ground to an Arduino Nano microcontroller. The microcontroller then activates a stimulator to apply electrical stimulus to subjects via gel electrodes. The stimulator consists of an H-bridge that converts DC supply voltage to biphasic stimulus by control signals from the microcontroller.

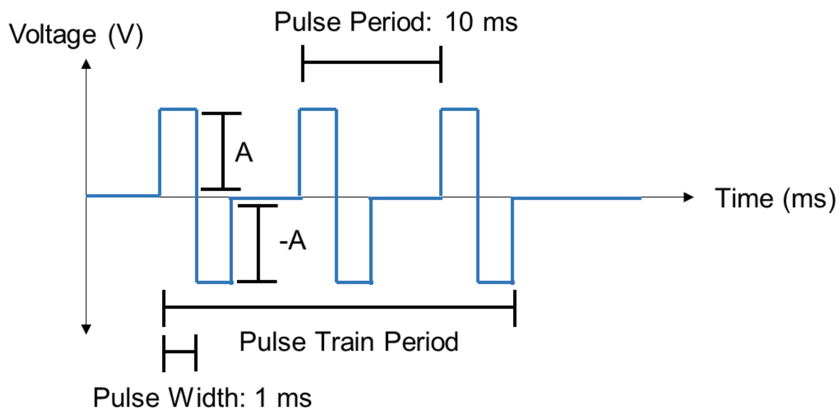


Figure 3: Biphasic Stimulation Provided to Subjects in Experiments

This diagram depicts the biphasic stimulation that was applied on the subjects' calcaneal and ulnar nerves during experimentation. When a subject crossed the threshold for stimulation on the board, the voltage of the stimulation always began at an amplitude of A. Then, 1 millisecond later, the voltage changed to -A for 1 millisecond, which created the biphasic waveform. The voltage amplitude (A) varied per subject and was determined before experimentation began. The delay time before the next pulse was 8 milliseconds, which created a 100 Hz frequency for stimulation. The pulse train period depended on the length of time that the subjects remained outside of the balanced region, and the stimulation ended once the subjects either returned to the balanced region or the balance board touched the ground.

Selection of Locations and Parameters for Transcutaneous Electrical Stimulation to Augment Plantar or Palmar Cutaneous Feedback

We established the location of electrodes and the stimulation voltage for each subject for both the plantar and palmar cutaneous augmentation via transcutaneous electrical stimulation. First, the subjects' skin was cleaned around the targeted electrode location with sterile alcohol prep pads to reduce the skin impedance. Then, the bipolar gel electrodes were placed along the expected pathways of target nerves on either the plantar or palmar surface (i.e., calcaneal nerve for plantar surface and ulnar nerve for palmar surface). Once the electrodes were in place, the voltage across the electrodes was raised from 0 V incrementally by 0.1 V until the subject reported that the stimulation evoked electrotactile feedback on the plantar or palmar surface. When the electrodes were not placed along the correct nerve, subjects reported electrotactile sensation around the electrodes instead of the plantar/palmar areas. We accordingly adjusted the location of electrodes until subjects reported plantar/palmar sensation. Subjects reported the level of sensation on a scale of 1 to 5, with 1 being minimal sensation and 5 being enough sensation to cause discomfort. We established the stimulation voltage to be utilized in experimentation when subjects reported 3 on the scale of 1 to 5. This process was completed for both feet and both hands for each subject because the location and threshold of stimulation can vary between sides of the body.

Sensory Deficit During the Balance Board Test

During the whole experiment, we introduced two kinds of sensory deficit. First, a piece of 10 cm-thick medium-density foam was placed between each subject's feet and the balance board to attenuate the plantar cutaneous feedback. This was done to emulate the condition of reduced plantar cutaneous feedback that is experienced by individuals with PN and elderly people. Additionally, subjects were asked to close their eyes to remove visual feedback, which presents a further challenge for subjects to balance on the balance board and increases the subjects' dependency on tactile information during the experiments. As subjects were healthy, young individuals, we expected that the balance board itself may not be enough to provide a challenging condition for balance.

Cognitive Intervention on the Balance Board Test

To determine the effect of cognitive involvement on the efficacy of sensory augmentation, we employed a cognitive intervention during the experiment. As a cognitive intervention, subjects were asked to continuously count backwards by 7 from a random two-digit number that was given by the operator at the beginning of each balance board trial (right before subjects released their hands from the handrail).

Balance Test on the Balance Board with Closed-loop Tactile Augmentation on Either the Foot Sole or the Palm

With all preparations of balance board, handrail, optical motion capture system, closed-loop tactile augmentation system, sensory interventions, and cognitive intervention, subjects participated in the balance board experiment. Each subject was instructed to stand on the lateral balance board barefoot with both feet equidistant from the center of the board and at shoulder width apart. Once correctly positioned on the board, subjects then gained their balance with the help of a stationary handrail affixed to the ground in front of the balance board. Subjects were then asked to close their eyes and release the handrail, move their hands to the sides of their body, and remain balanced on the board for as long as possible. The duration of time that a subject was able to maintain balance on the board without the board touching the ground was termed the balance time for this study.

Subjects participated in the balance board test through two separate visits on two different days. During the first visit, half of the subjects were given the following three different conditions: 1) no stimulation (control), 2) stimulation onto the medial calcaneal nerve (tactile augmentation from the foot sole), and 3) stimulation onto the medial calcaneal nerve plus a cognitive task (counting backward). At the second visit, they were given the following three different conditions: 1) no stimulation (control), 2) stimulation onto the ulnar nerve (tactile augmentation from the palm), and 3) stimulation onto the ulnar nerve plus a cognitive task (counting backward). The other half of the subjects were given the augmentation in a reverse order (palmar augmentation during the first visit and plantar augmentation during the second visit).

During each visit, subjects participated in four sessions, each composed of 30 trials. Subjects were instructed to rest for five seconds between trials in order to minimize the effect of fatigue. Between each session of the experiment, subjects were also given five minutes to sit and rest. In each trial, each of the three conditions were given in a random order (10 trials for each condition) to eliminate any learning effect. The timeline for the experimental design of each visit is summarized in Fig. 4.

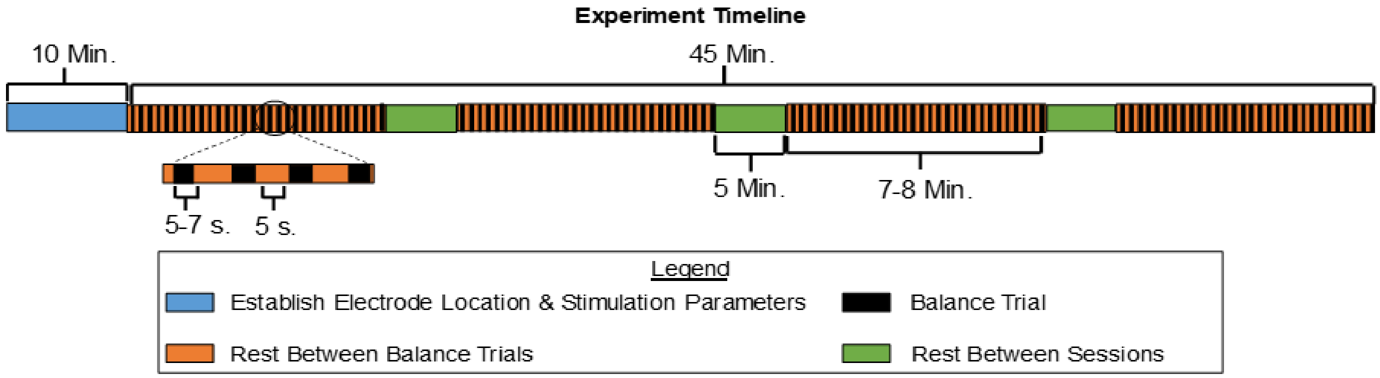


Figure 4: Experimental Timeline

Timeline of the palmar and plantar sensory augmentation experiments. The first 10 minutes of either experiment is used to establish the location of the electrodes and the thresholds of stimulation for the subject, for tactile feedback to be augmented via transcutaneous electrical stimulation on either the palmar or plantar surface. The experiments are broken up into 4 sessions that each contain 30 balance trials. After each trial, the subject rests for 5 seconds to avoid fatigue. The subject also rests by sitting down for 5 minutes between each session. Each trial can last approximately 5 to 7 seconds, which incorporates time for the subject to gain his or her balance with the use of the handrail, receive a verbal cue to release the rail and begin the trial, and the time they are able to keep their balance.

Data Analysis Using Marker Position Data from the Balance Board

The data collected on the lateral balance board via the Optitrack motion capture system provided us with detailed information of the subjects' balancing ability. Although balance time works as a good indicator of the postural regulation, the subjects' movement during the balancing tasks is important information as well. The optical markers, placed on each end of the balance board, allowed us to analyze the three-dimensional movement of the board by providing the markers' unique, three-dimensional coordinates at 120 Hz with sub-mm precision.

We first measured the number of *threshold crossings per session*. This measure indicates how often subjects lost their balance and then returned back to the balanced position on a session basis. Each threshold crossing indicates that one side of balance board was more than 1.5 cm vertically below the perfectly balanced position. By averaging the number of threshold crossings that happened for each intervention, we have an indicator of how many times the subjects were able to deviate from and return to a balanced position, which informs us of how well they were able to control their balance.

We also measured the amount of *deviation per threshold crossing*. This measure indicates how well subjects could respond to a deviation away from the balanced position. To determine the amount of deviation per threshold crossing, we calculated the average area under the curve between time and board marker position in the vertical direction. We first integrated the area under the curve between time and marker position. We then divided the total area by the total number of threshold crossings to produce the average area per threshold crossing for the entire subject group. This calculation, which is detailed in Eq. 1, was grouped according to the method of intervention applied during experimentation so that each method could be compared. A larger amount of deviation per threshold crossing indicates that subjects required a larger deviation to regain their balance, or their response time was slower, or a combination of the two cases. Thus, a smaller average area per stimulation threshold crossing indicates that subjects regained their balance better, and therefore did not deviate much from the balanced position.

$$avg.\,deviation\ area = \frac{\sum_{i=1}^{d} \int_{t,crossing}^{t,return} board\ position\ dt}{total\ threshold\ crossings}\ ,(1)$$

d = total number of threshold crossings

Finally, we measured *the average deviation time* of each subject for all trials in the experiments. The average deviation time is a measurement of how much time on average the balance board was outside of the window of balance between 7 and 10 cm. In other words, the deviation time indicates how quickly a subject could respond to stimuli, either natural or augmented, and return to a balanced position. In our terminology, we defined a deviation is an occurrence of a subject crossing the threshold for simulation in either direction. The average deviation time duration provides insight into how much time the subjects were off-balance and were receiving stimulation, with the exception of the trials performed with no stimulation. Average deviation time is helpful for quantifying how well the subjects were able to return to a balanced position throughout the trials and will be used to determine which, if any, interventions helped to improve balance.

The metrics used in this study to determine the effectiveness in balance improvement of each intervention are further explained in Fig. 5. In this figure, an example of the marker board data that we recorded during the balance trial is shown, as well as indicators for key moments during the example trial.

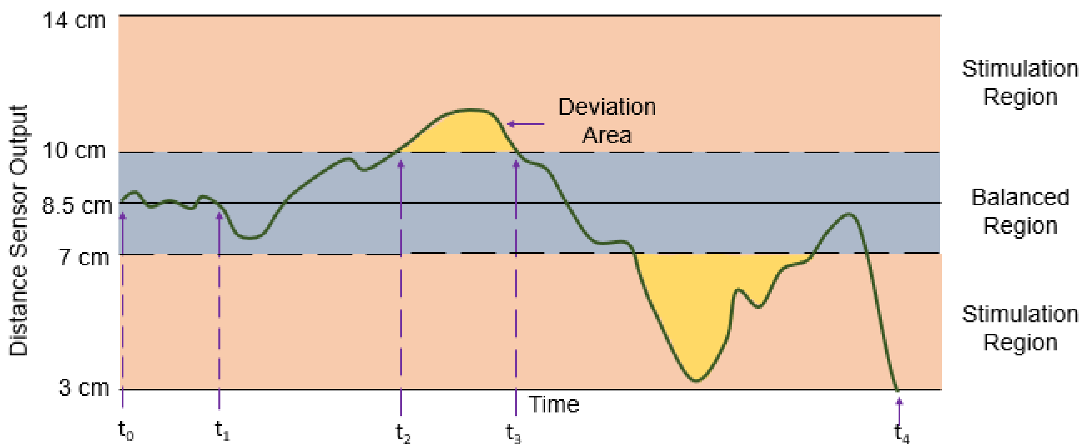


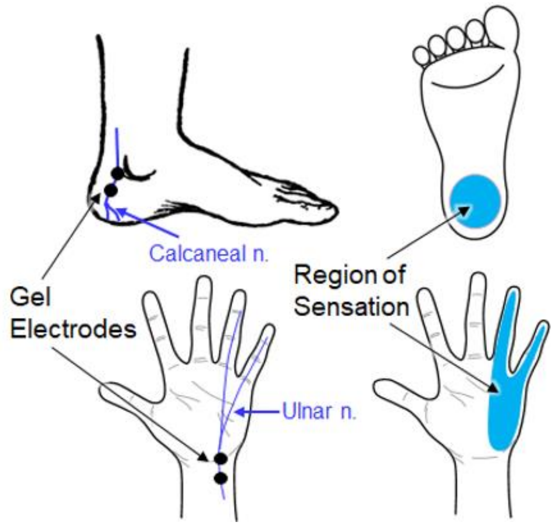
Figure 5: Example Raw Data from Balance Board Markers

Example balance board marker data during the balance experiments. The example data demonstrates the output of the optical markers on the balance board in the vertical direction. We utilized this data to evaluate how well each subject was able to regulate their balance throughout the trials of the experiments, which either confirmed or denied if each intervention type was successful in aiding postural regulation. The five points in time are defined as follows: t0 occurs when the subject gains their balance with the help of the handrail, t1 occurs when the subject releases the handrail to begin the trial, t2 occurs when the subject crosses a stimulation threshold (right side of board high and left side low) and stimulation is applied (except during control trials), t3 occurs when the subject returns to the balanced region and stimulation is turned off, t4 occurs when the balance board touches the ground to conclude the trial, t4 – t1 is the balance time, and t3 – t2 is the deviation time.

CHAPTER III EXPERIMENTAL RESULTS

Plantar and Palmar Tactile Feedback could be Evoked by Transcutaneous Electrical Stimulation for All Subjects

The locations of the gel electrodes used for tactile augmentation on the foot sole and the palm are depicted in Fig. 6a. Electrical stimulation that was applied onto the posterior and inferior side of the medial malleolus, where the medial calcaneal nerve is located, augmented tactile feedback from the heel of the foot sole. Electrical stimulation applied onto the lateral and anterior side of the wrist, where the ulnar nerve is located, augmented tactile feedback from the lateral side of the palm on the ring and pinky fingers (fourth and fifth fingers). The artificial tactile feedback was evoked onto the areas depicted in Fig. 6b, for the foot sole and the palm, respectively. The stimulation voltages required to evoke artificial tactile feedback, at a level of 3 out of 5 (as reported by each subject), are shown in Fig. 7 for hand stimulation and in Fig. 8 for foot stimulation. No subject reported feeling any discomfort by the stimulation at the selected voltage.



(a) (b)

Figure 6: Placement of Electrodes and Region of Sensation for Tactile Augmentation

Depiction of electrical stimulation through gel electrodes along the calcaneal and ulnar nerves: (a) location of get electrodes and (b) area where the artificial sensory feedback was evoked.

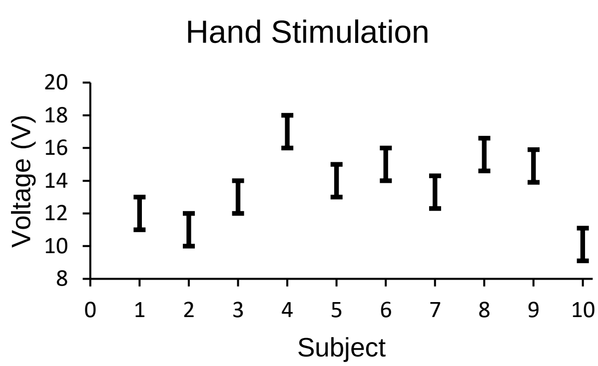


Figure 7: Voltage Level Used for Palmar Stimulation

Voltage levels required to produce reasonable augmented sensation on the palm of the hand, as reported by each subject.

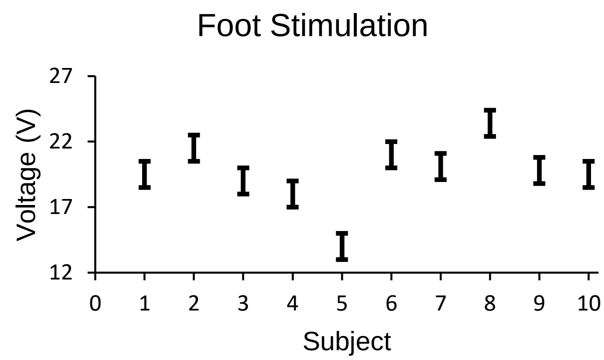


Figure 8: Voltage Level Used for Plantar Stimulation

Voltage levels required to produce reasonable augmented sensation on the foot sole, as reported by each subject.

Average Balance Time Results

The average balance time results of the sensory augmentation experiments are graphically represented in Figs. 9 and 10. In Fig. 9, the average balance times for all subjects that partook in the hand stimulation experiment are shown for each of the three intervention methods. The data shows that there is a significant increase in the average balance time when the subjects were given sensory augmentation on the palmar surface as compensatory sensory cue, when compared to the control setting of no stimulation. When no stimulation was given, the average balance time was 2.247 s, whereas the average balance time was 2.421 seconds when compensatory sensory augmentation was applied on the palm. Additionally, when a cognitive task was given in conjunction with the palmar stimulation, the average balance time was 2.246 s, which is nearly identical to the control setting.

Fig. 10 depicts the balance time information that corresponds to the foot stimulation experiment. The average balance times of the subjects when no stimulation was given was the lowest of the three intervention methods at 2.190 s. When stimulation was applied to the plantar surface as a sensory cue, the average balance time was 2.286 s, which is slightly longer than when no stimulation was given. Finally, when foot stimulation was applied along with a cognitive task, the average balance time was 2.483 s. With the cognitive task was present along with stimulation, the average balance time was 0.197 s longer than when only stimulation was present and 0.264 s longer than when no stimulation was applied.

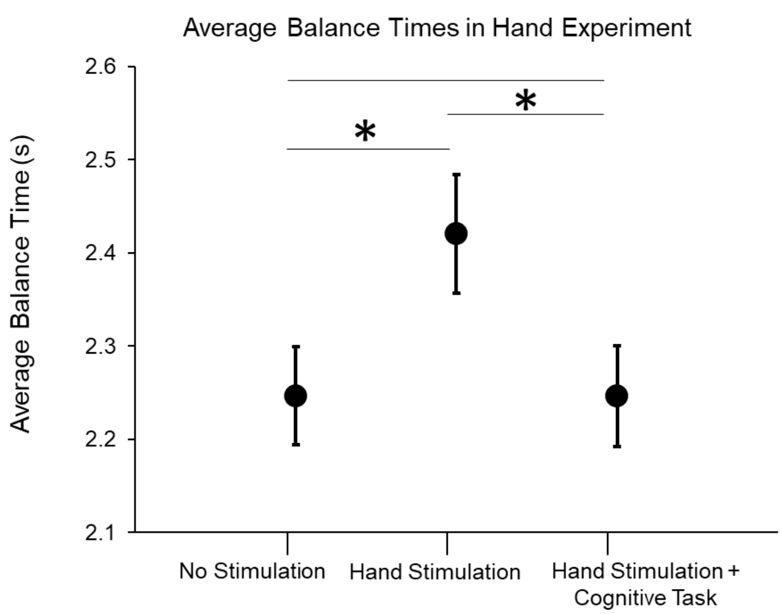


Figure 9: Average Balance Times for Hand Experiment

Average balance times for all subjects in the experiment of sensory augmentation on the hand. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

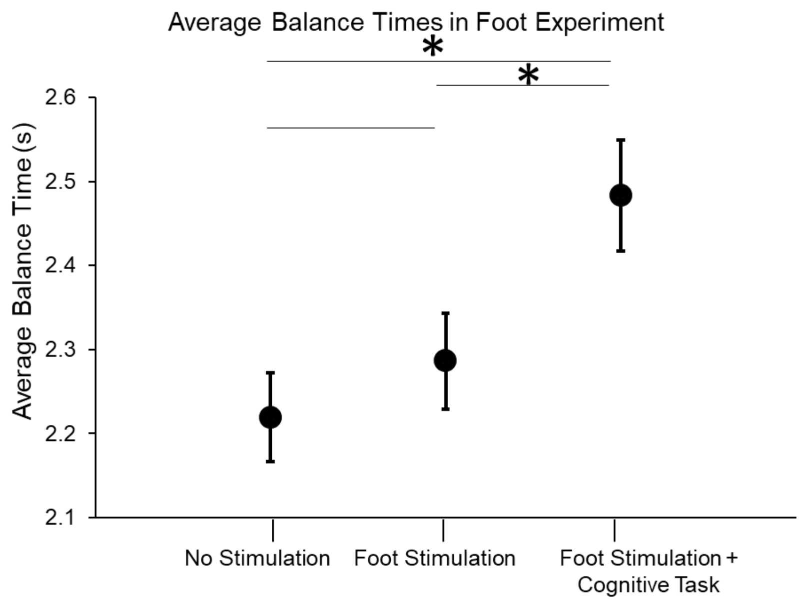


Figure 10: Average Balance Times for Foot Experiment

Average balance times for all subjects in the experiment of sensory augmentation on the foot. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

Threshold Crossings Results

The number of threshold crossings was grouped by intervention type and averaged per session for the entire subject population. In Fig. 11, the average number of threshold crossings per session is plotted for the hand stimulation experiment, and Fig. 12 contains the same metric for the foot stimulation experiment. For the hand experiment, the average number of stimulation threshold crossings per session is 24.27 for the trials with stimulation applied to the hand, which is 2.77 more than when no stimulation was applied and 2.86 more than when stimulation was given along with a cognitive task. The average number of stimulation threshold crossings per session in the foot experiment is 24.65 for the trials with foot stimulation and a cognitive task given, which is 3.35 more than when no stimulation was given and 2.69 more than when stimulation was given without a cognitive task.

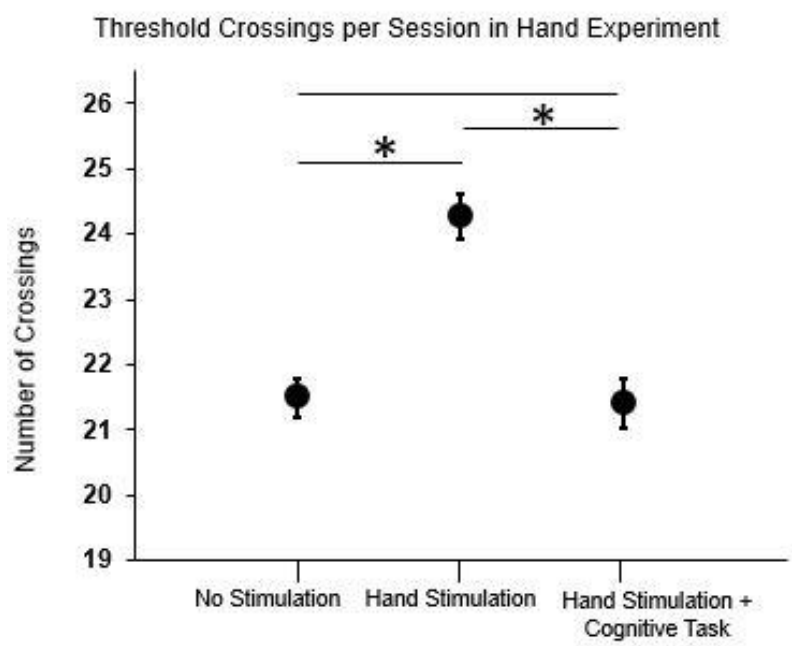


Figure 11: Average Threshold Crossings per Session in Hand Experiment

Average number of threshold crossings for all subjects in the experiment of sensory augmentation on the hand. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

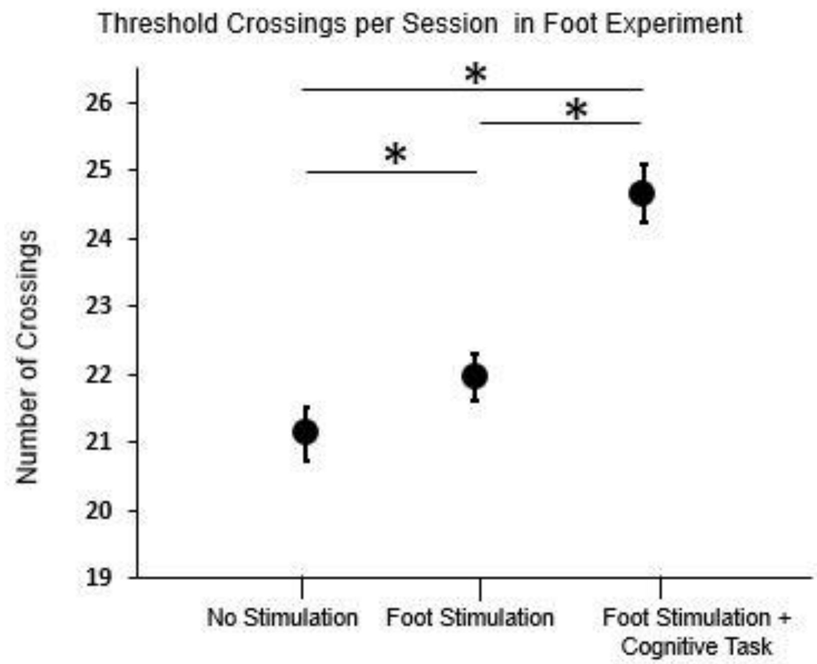


Figure 12: Average Threshold Crossings per Session in Foot Experiment

Average number of threshold crossings for all subjects in the experiment of sensory augmentation on the foot. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

Average Deviation Area per Crossing Results

In Fig. 13, the average deviation area per stimulation threshold crossing is plotted for all three intervention methods in the hand stimulation experiment, and the corresponding data for the foot stimulation is plotted in Fig. 14. In the hand experiment, the average area per stimulation threshold crossing is very similar for all three intervention methods, with none being significantly different from each other. In the experiment with stimulation along the calcaneal nerve, the average deviation area per crossing was largest with no stimulation present, at a value of 1.456 mm·s. With foot stimulation alone, the average deviation area is reduced to 1.369 mm·s, and it is further reduced to 1.352 mm·s when a cognitive task was given along with the foot stimulation.

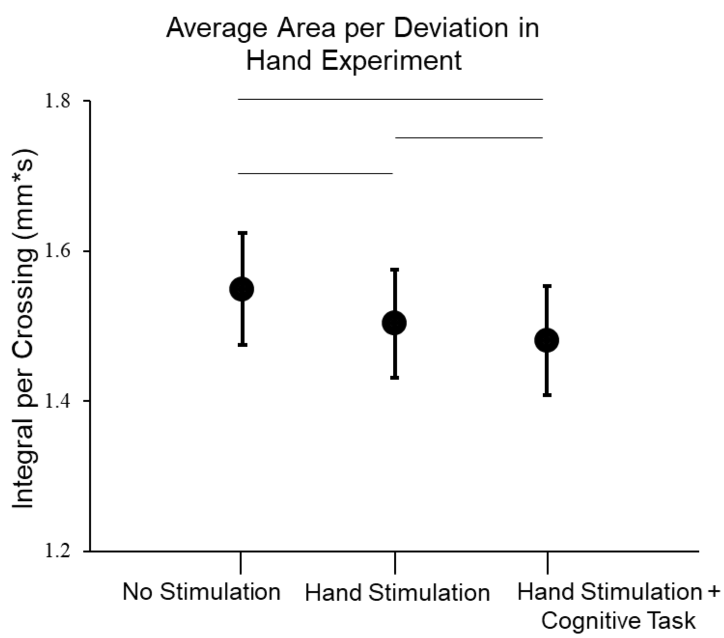


Figure 13: Average Deviation Area per Threshold Crossing in Hand Experiment

Average deviation area per threshold crossing for all subjects in the experiment of sensory augmentation on the hand. Data points are shown with ± Standard Error (SE). Asterisks indicate p < 0.05 by two-tailed paired T-test.

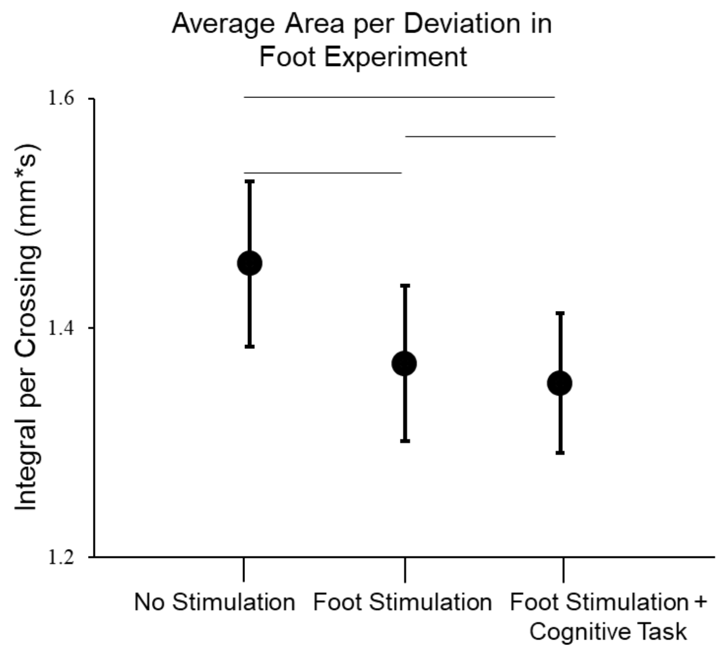


Figure 14: Average Deviation Area per Threshold Crossing in Foot Experiment

Average deviation area per threshold crossing for all subjects in the experiment of sensory augmentation on the foot. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

Average Deviation Time Results

The deviation time per threshold crossing was grouped by intervention type and averaged for the entire subject population. In Fig. 15, the average deviation time per threshold crossing is plotted for the hand stimulation experiment, and Fig. 16 contains the same metric for the foot stimulation experiment. For the hand experiment, the average deviation time per crossing very similar for all three intervention methods, with each method producing an average deviation time of about 0.61 seconds. The results of the foot stimulation experiment follow a similar trend to the hand stimulation experiment. The average of deviation time per crossing in the foot experiment is 0.60 seconds for the trials with no stimulation, which is 18.7 milliseconds greater than when stimulation was given with a cognitive task.

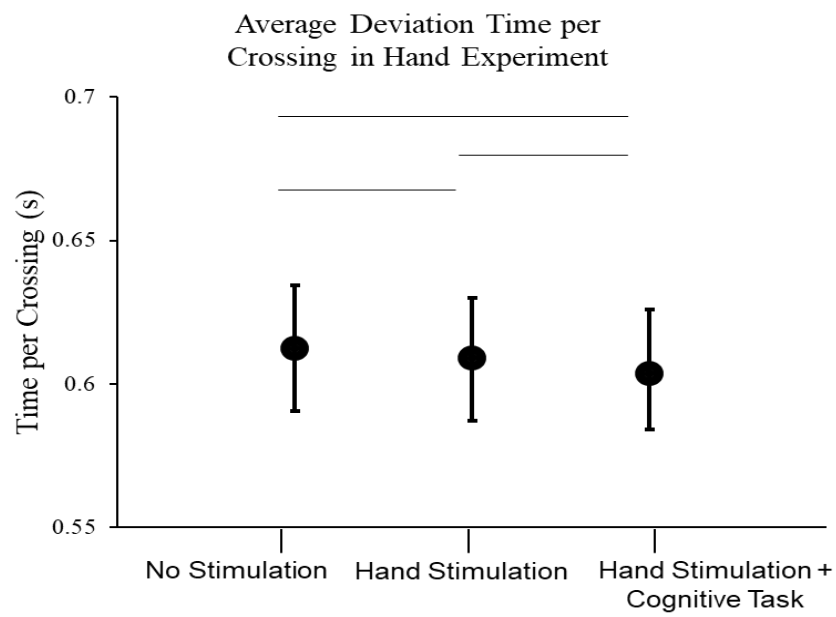


Figure 15: Average Deviation Time per Threshold Crossing in Hand Experiment

Average deviation time per threshold crossing for all subjects in the experiment of sensory augmentation on the hand. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

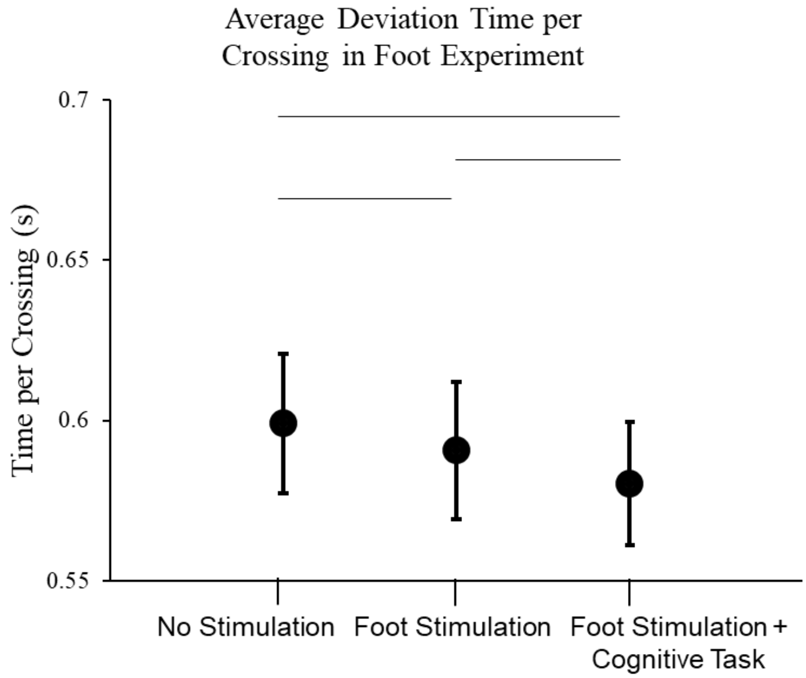


Figure 16: Average Deviation Time per Threshold Crossing in Foot Experiment

Average deviation time per threshold crossing for all subjects in the experiment of sensory augmentation on the foot. Data points are shown with ± Standard Error (SE). Asterisks indicate $p < 0.05$ by two-tailed paired T-test.

CHAPTER IV DISCUSSION

Sensory Augmentation via Transcutaneous Electrical Nerve Stimulation is Viable for Individuals with Peripheral Neuropathy

From the findings in the stimulation location and threshold experiment, we determined that both plantar and palmar stimulation along the calcaneal nerve and ulnar nerve can be elicited with ease in a safe, non-invasive, unobtrusive, and accurate manner. These results indicate that an individual with peripheral neuropathy would be able to feel augmented sensations similar to what their natural sensation was before their injury or disorder when this type of stimulation is applied. Thus, this population of individuals can participate in future studies similar in nature to the balance experiments of this study in order for us to investigate the effect of sensory augmentation on the postural regulation of the target individuals. Additionally, these findings are important for a potential wearable version of the stimulator to be made and put into practice as an assistive device.

Mediolateral Balance is Improved by Augmented Sensation on the Palmar and Plantar Surface

As shown in Figs. 9 and 10, an improvement in baseline mediolateral balance on the balance board was achieved with electrical stimulation of both the ulnar and calcaneal nerve, with the improvement achieved through palmar stimulation being significant. This means that the subjects were able to interpret the given sensory cues when their balance strayed from a median position, and then they acted upon these cues to shift their weight in a manner that allowed them to stay balanced on the board longer than when they relied solely on the limited tactile sensation on their feet.

This improvement in mediolateral balance with reduced plantar surface feedback was accomplished in a challenging environment. Thus, it follows that sensory augmentation on both the plantar and palmar surfaces are capable of improving postural regulation in less complex environments, such as standing or walking. Therefore, either modality of sensory augmentation could be utilized to mitigate the risk of falls due to poor balance for individuals that suffer from peripheral neuropathy, and palmar augmentation would achieve the largest improvement in balance for these individuals.

Improved Balance Correlates to more Threshold Crossings

From the average balance time data, it was determined that both plantar and palmar sensory augmentation allowed subjects to maintain their balance on the balance board for a longer period of time. This metric of evaluation demonstrates improved balance on a large scale. To understand the minute improvements in balance that lead to more time spent on the balance board, we focus on the number of stimulation threshold crossings per session. When sensory augmentation was given, regardless of the location of the augmentation, the stimulation threshold crossings per session increased when compared to the control situation in which no stimulation was provided to the subjects. This indicates that subjects were able to balance longer when provided with sensory cues simply by regaining their balance more times than when they were forced to rely only on their reduced tactile sensation alone.

The strong correlation between balance time and stimulation threshold crossings per session is further proven from the recorded data for trials that involved sensory augmentation plus the cognitive task. In the hand stimulation experiment, introducing the cognitive task shifts the number of stimulation threshold crossings per session to nearly the exact number of crossings when no stimulation was present, which matches the trend in balance times from this experiment. Furthermore, in the foot stimulation experiment, the presence of the cognitive task increases the number of stimulation threshold crossings per session by 12.2% compared to the number of crossings with stimulation alone. This increase in crossings mirrors the 8.7% increase in average balance time from the stimulation trials to the stimulation plus cognitive task trials. Thus, we conclude that there is a definitive correlation between the number of stimulation threshold crossings per session and balance time on the lateral balance board. This finding suggests that the interventions that helped to improve balance did so by cueing subjects to shift their weight back and forth without shifting too far from the median position, which allowed them to avoid contact with the ground for a longer time than they could without these cues.

Balance is Improved by Minimizing Average Deviation Area

For a further understanding of the efficiency of each intervention method used in our experiments, we investigate the average deviation area per threshold crossing metric of balance evaluation. A reduction in the average deviation height per threshold crossing is an indication that a subject remained closer to the balance window when they crossed the threshold for stimulation when compared to a larger deviation area, or that they decreased the average deviation distance from the balanced region, or they achieved a combination of the two. To do this when sensory cues are given signifies that a subject is responding to the stimulus more efficiently than when depending on reduced tactile sensation of the foot alone and is demonstrating a more precise control of their balance. This is exactly the case in the foot stimulation experiment, in which stimulation alone reduces the average area per threshold crossing, and foot stimulation plus the cognitive task further reduces it. In the hand experiment, the average deviation area with the control intervention was reduced by palmar sensory augmentation with and without the cognitive task, but this reduction was very minimal. From this data set, we deduce that the more efficient method of intervention is sensory augmentation on the plantar surface because the data suggests that subjects are able to consciously and subconsciously incorporate the plantar augmentation to control their balance more precisely and respond to perturbations faster than they can with palmar augmentation.

Response Time is Improved by Plantar Augmentation

From the average balance time data, it was determined that both plantar and palmar sensory augmentation allowed subjects to maintain their balance on the balance board for a longer period of time. This metric of evaluation demonstrates improved balance on a large scale. To understand the minute improvements in balance that lead to more time spent on the balance board, we focus on the average deviation time per threshold crossings. In the experiments in which palmar augmentation was given, the average deviation time was nearly identical regardless of the intervention method. This result is interesting because the average balance time was significantly improved by palmar augmentation, but clearly this improvement in balance time was not accomplished by a reduction in deviation time. However, in the plantar augmentation trials, there is a correlation between a reduction in deviation time and an increase in balance time. This correlation holds true for both the plantar stimulation alone and the plantar stimulation with a cognitive task. From this correlation, we deduce that the postural regulation of the subjects was improved via plantar augmentation, at least in part, due to a slightly faster response time to stimulus.

Location of Sensory Augmentation Accesses Different Sensory Pathways

As discussed in Fig. 1, both palmar and plantar sensory information can be process by the pre-frontal cortex to influence motor output. Because the average balance time for the subject group was larger when stimulation was applied at either location than the balance time with no stimulation, we can deduce that both direct stimulation (on the foot) and indirect stimulation (on the hand) have a positive effect on balance when prefrontal cortical processing is not preoccupied with a cognitive task. This finding is in line with other studies that found compensatory sensory cues to be helpful in balancing tasks [6-9].

It is an unsurprising result that giving an overt sensory cue allows for individuals with limited postural feedback (i.e., visual feedback removed and tactile feedback reduced) to cognitively interpret the cue and react appropriately to improve their balance. However, very interestingly, when the prefrontal cortex is focused on the cognitive task, hand stimulation evokes no improvement in balance time, whereas the foot stimulation actually elicits further improvement in balance time than foot stimulation alone with no cognitive task. Additionally, plantar augmentation allowed for a reduction in both the deviation time and the average deviation area when compared to no stimulation, which indicates that the plantar augmentation was incorporated naturally by the balance regulation system of the cerebellum. Whereas, palmar stimulation only allowed for a minimal reduction in deviation area but had no effect on response time to deviation, and a cognitive task eliminated any benefit on balance that the palmar stimulation introduced. This result indicates that the palmar stimulation indeed was only processed via the pre-frontal cortex and was not incorporated into the balance regulation system in the cerebellum. These findings reinforce the idea of shared resources for motor and cognitive functions because the motor output of the body's balancing mechanism was hindered when subjects were focused on the cognitive task in the hand stimulation experiment, and sensory input from the hand is processed solely in the pre-frontal cortex for the balancing task [28].

This finding also suggests that the sensory input from the plantar surface is very faintly associated or not associated at all to cognitive function because the cognitive task did not hinder the subjects' ability to balance better when they were occupied with a cognitive task. The notion of cognitive distraction as a means to learning in a postural task by involving more automatic mechanisms has been suggested before, but has not been comprehensively studied [29]. It is possible that this method of learning occurred in this study. Note that, as shown in Fig. 6b, the selected transcutaneous electrical nerve stimulation in this study evoked sensation from only a portion of the area of the foot sole or the palm, and we believe that the corresponding experimental results provide important information regarding the effectiveness of tactile augmentation on postural balance.

These important findings suggest that both plantar and palmar augmentation can improve mediolateral balance when the pre-frontal cortex is allowed to focus on the sensory cues. Additionally, the findings suggest that augmented plantar cutaneous sensation is more effective at improving balance when sensory cues are handled subconsciously by the intrinsic sensorimotor pathway associated with balance through the cerebellum. This result, combined with the result that augmented palmar cutaneous feedback was only effective at improving mediolateral balance when no cognitive task was present, suggests that plantar augmentation may be an ideal modality to improve postural regulation for people with a balance deficit. Ultimately, this finding should shift our attention to augmented plantar sensation as the target area of interest in future studies on rehabilitation and assistive efforts to improve postural regulation in individuals with peripheral neuropathy.

CHAPTER V CONCLUSIONS

In this thesis, we presented a novel plantar cutaneous augmentation approach by a closed-loop transcutaneous distal-tibial nerve stimulation. The closed-loop distal-tibial nerve stimulation could enhance agility in responding to the body sway and increase balance time. In our study, the importance of plantar cutaneous augmentation became noticeable, especially at cognitively-challenging situation. We also detailed the improved efficacy of plantar cutaneous augmentation over compensatory approaches to the improvement of balance deficit, such as palmar augmentation. This new sensory augmentation approach via the distal-tibial nerve can directly address the lack of plantar cutaneous feedback for those with PN, while maintaining the potential high usability as a non-pharmacologic and non-invasive solution.

APPENDIX A: ARDUINO CODE

The following code, written in the Arduino programming language, was utilized to do two things: 1) record the balance times in the experiments of this study and 2) monitor the position of the lateral balance board and apply stimulation to the subjects based off the board's position.

The code is as follows:

```
"// This sketch tracks the timing of trials while also providing stimulation
// based on information from the proximity sensor

const int TRIG_PIN_LEFT = 7;
const int ECHO_PIN_LEFT = 8;
const int ELECTRODE_1_PIN = 2;
const int ELECTRODE_1_GND = 3;
const int ELECTRODE_2_PIN = 11;
const int ELECTRODE_2_GND = 12;
int push_button_1 = 6;
int push_button_2 = 5;
int left_board_sensorPin = 14;     // select the input pin for the force sensor on left side of
board
int left_hand_sensorPin = 15;    // select the input pin for the force sensor on left hand
int right_hand_sensorPin = 16;   // select the input pin for the force sensor on left hand
int right_board_sensorPin = 18;     // select the input pin for the force sensor on right side
of board
int left_hand_threshold = 370;  // threshold value for force sensor
int left_board_threshold = 370;  // threshold value for force sensor
int right_hand_threshold = 350;  // threshold value for force sensor
int right_board_threshold = 430;  // threshold value for force sensor

int count = 0; //count of trial number
int greenLedPin = 19;   // select the pin for the LED
int yellowLedPin = 17;   // select the pin for the LED
unsigned long startTime;
unsigned long endTime;
unsigned long duration;
```

```
int timerRunning = 0;
int pushbutton1_val = LOW;
int pushbutton2_val = LOW;
int wait = 1;

// Anything over 400 cm (23200 us pulse) is "out of range"
const unsigned int MAX_DIST = 23200;

void setup() {
  pinMode (push_button_1, INPUT_PULLUP);
  pinMode (push_button_2, INPUT_PULLUP);
  pinMode(greenLedPin, OUTPUT);  // declare the greenLedPin as an OUTPUT
  pinMode(yellowLedPin, OUTPUT);  // declare the greenLedPin as an OUTPUT

  // The Trigger pins will tell the sensor to range find
  // Left sensor
  pinMode(TRIG_PIN_LEFT, OUTPUT);
  digitalWrite(TRIG_PIN_LEFT, LOW);
  pinMode(ECHO_PIN_LEFT, INPUT);        // sets the echo pin as input

  // Left electrode
  pinMode(ELECTRODE_1_PIN, OUTPUT);
  pinMode(ELECTRODE_1_GND, OUTPUT);

  // Right electrode
  pinMode(ELECTRODE_2_PIN, OUTPUT);
  pinMode(ELECTRODE_2_GND, OUTPUT);


  Serial.begin(9600);
}

void loop() {

  while (wait == 1) {
    if (digitalRead(push_button_1) == HIGH && (analogRead(left_hand_sensorPin) > left_hand_threshold
        || analogRead(right_hand_sensorPin) > right_hand_threshold)) { //start experiment with push button 1 and hand on force sensor
      digitalWrite(yellowLedPin, HIGH);
      wait = 0;
    }
  }
```

```
 if (analogReadleft_hand_sensorPin) < left_hand_threshold &&
analogRead(right_hand_sensorPin) < right_hand_threshold && timerRunning == 0 &&
   analogRead(left_board_sensorPin) < left_board_threshold &&
analogRead(right_board_sensorPin) < right_board_threshold) { //hands off sensors &
board still up & timer not running already
  startTime = millis();
  timerRunning = 1;
  digitalWrite(greenLedPin, HIGH);  // turn the greenLedPin on
  digitalWrite(yellowLedPin, LOW);
  while ( analogRead(left_board_sensorPin) < left_board_threshold &&
analogRead(right_board_sensorPin) < right_board_threshold) { //keep running till board
touches ground
   // left parameters
   unsigned long t1_left;
   unsigned long t2_left;
   unsigned long pulse_width_left;
   float cm_left;

   // Hold the trigger pin high for at least 10 us
   // left
   digitalWrite(TRIG_PIN_LEFT, HIGH);
   delayMicroseconds(10);
   digitalWrite(TRIG_PIN_LEFT, LOW);

   // Wait for pulse on echo pin
   while ( digitalRead(ECHO_PIN_LEFT) == 0 );

   // Measure how long the echo pin was held high (pulse width)
   // Note: the micros() counter will overflow after ~70 min
   t1_left = micros();
   while ( digitalRead(ECHO_PIN_LEFT) == 1);
   t2_left = micros();
   pulse_width_left = t2_left - t1_left;

   // Calculate distance in centimeters and inches. The constants
   // are found in the datasheet, and calculated from the assumed speed
   //of sound in air at sea level (~340 m/s).
   cm_left = pulse_width_left / 58.0;

   // Print out results
   if ( pulse_width_left > MAX_DIST ) {
    //Serial.println("Out of range");
   } else {
```

```
      //Serial.print(cm_left);
      //Serial.print(" cm on left \t\t\t\t\n");
    }

    if ( cm_left < 7) {
      for (int i = 0; i <= 6; i++) {
        digitalWrite(ELECTRODE_1_PIN, HIGH);
        digitalWrite(ELECTRODE_1_GND, LOW);
        delay(1);
        digitalWrite(ELECTRODE_1_PIN, LOW);
        digitalWrite(ELECTRODE_1_GND, HIGH);
        delay(1);
        digitalWrite(ELECTRODE_1_PIN, LOW);
        digitalWrite(ELECTRODE_1_GND, LOW);
        delay(8);
      }
    }
    else if (cm_left > 10) {
      for (int i = 0; i <= 6; i++) {
        digitalWrite(ELECTRODE_2_PIN, HIGH);
        digitalWrite(ELECTRODE_2_GND, LOW);
        delay(1);
        digitalWrite(ELECTRODE_2_PIN, LOW);
        digitalWrite(ELECTRODE_2_GND, HIGH);
        delay(1);
        digitalWrite(ELECTRODE_2_PIN, LOW);
        digitalWrite(ELECTRODE_2_GND, LOW);
        delay(8);
      }
    }
    else {
      for (int i = 0; i <= 6; i++) {
        digitalWrite(ELECTRODE_1_PIN, LOW);
        digitalWrite(ELECTRODE_1_GND, LOW);
        digitalWrite(ELECTRODE_2_PIN, LOW);
        digitalWrite(ELECTRODE_2_GND, LOW);
        delay(10);
      }
    }
  }

}
```

```
  if (timerRunning == 1 && (analogRead(left_board_sensorPin) > left_board_threshold || analogRead(right_board_sensorPin) > right_board_threshold)) { // timer running, board on ground
    endTime = millis();
    timerRunning = 0;
    digitalWrite(greenLedPin, LOW);   // turn the greenLedPin off
    wait = 1;
    count++;
    duration = endTime - startTime;
    Serial.print ("experiment time in milliseconds: ");
    Serial.println (duration);
    Serial.print ("trial number: ");
    Serial.println (count);

  }

}"
```

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