DISSERTATION

BAYES'D AND CONFUSED: NOVEL APPLICATIONS OF BAYESIAN INFERENCE TO BETTER UNDERSTAND SENSORIMOTOR UNCERTAINTY

Submitted by

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ABSTRACT

BAYES'D AND CONFUSED: NOVEL APPLICATIONS OF BAYESIAN INFERENCE TO BETTER UNDERSTAND SENSORIMOTOR UNCERTAINTY

Effective motor control relies on accurate sensory information. However, sensory information is inherently variable and clouded with uncertainty. Yet, humans perform motor skills with a high degree of proficiency and reliability. How the central nervous system (CNS) controls motor function amid the uncertainty of sensory signals is not known. Researchers in recent years have suggested that the brain may control movement in a way that can be explained by Bayesian inference. Bayesian inference posits that the most probable outcome is the product of both the currently available data (sensory information) as well as previously collected data (learned expectations). Applying Bayesian inference to a motor control context, we suggest that the CNS accounts for the uncertainty in sensory information by filling in the gaps of uncertainty with learned expectations when forming beliefs on where our body parts are in space. While initial findings on this topic are promising, they predominantly involve one-dimensional upper-body tasks. The purpose of this dissertation was to determine if Bayesian model of sensorimotor control is consistent in a full body stepping movement and if it can be further utilized to understand sensory function in various contexts. The first study in this dissertation was done to discover if the center of mass (CoM) position is estimated in a Bayesian way during stepping, like what has been shown in upper body movements. The second study sought to identify if Bayesian position estimations are beneficial to overall motor performance. In the third study, we applied what we have discovered about Bayesian inference in full body movements to understand the effects of transcutaneous electric nerve stimulation (TENS) on positional awareness during motor control. We hope to build on these findings to better understand how sensory information is utilized by the CNS to control movement.

DEDICATION

To Baby Shark, do doo d-doo d-doo.

TABLE OF CONTENTS

CHAPTER 1 – SOMATOSENSORY INFORMATION IN SKILLED MOTOR PERFORMANCE

Introduction

Whether restoring movements that have been impaired by disease or injury, offsetting the mobility deficits that accompany the aging process, or gaining competitive advantage, a common goal shared by many populations is to improve movement execution. As a result, people dedicate much time and money to enhance their ability to move effectively. Goal-oriented movements are the result of many electric signals sent from the central nervous system (CNS) to cause contraction of muscles in the periphery. Because it is the contraction of muscle that creates movement, most interventions and training protocols are employed to specifically improve muscle functions such as resistance training, cardiovascular exercise, or flexibility training (Cadore, Rodríguez-Mañas, Sinclair, & Izquierdo, 2013; Gunn, Markevics, Haas, Marsden, & Freeman, 2015a; Lloyd et al., 2016b; Mak, Wong-Yu, Shen, & Chung, 2017; Pogrebnoy & Dennett, 2020). Undeniably, the contributions of a healthy muscular system play a significant role in the emergence of functional and adaptive movement. Accordingly, it is no surprise that many of these training regiments lead to positive results in improving mobility. However, the somatosensory feedback accompanying motor activity is essential towards effective movement as well. Just as a dirty windshield limits the success of a high-end sports car, sensory information dictates the efficacy of goal-directed movements.

The purpose of this Introduction is threefold: First, I aim to emphasize the vital role of somatosensory information in the performance of skilled motor performance. To address this first aim, I discuss evidence from the fields of neuroanatomy, bioenergetics, and computational motor control that, taken together, emphasizes the role of sensory information in movement control. The second aim is to emphasize the need for careful intention in identifying the appropriate methods utilized to study or assess somatosensation's role in skilled motor performance. The final aim of the Introduction is to call attention to possible intervention approaches that show promise for improving motor performance specifically by targeting somatosensory function.

I will begin by discussing the process that leads to the firing of sensory receptors in the periphery and the transmission of sensory data to supraspinal areas of the CNS. Following this discussion, I will lay out three essential neural calculations involved in sensory processing that enable effective movements and provide evidence from different areas of research that illustrate their importance.

The motor control problem

Controlling successful movements is an intricate process. Accordingly, the responsibility of planning, coordinating, and executing a movement is no small task. The neuromuscular system contains an overwhelming number of biomechanical elements known as degrees of freedom (DOF) (Bernstein, 1945). These DOF allow us to make dexterous, adaptable movements with smoothness and precision. However, this complexity also introduces an infinite number of possibilities when creating and executing a movement plan. To ensure that a proper movement is executed, the CNS relies on sensory information to deliver timely updates on the current state of the body and the environment before, during and after a movement is executed. Even so, this process of using sensory information to inform motor decisions is far from perfect.

All afferent information is accompanied by unavoidable uncertainty (Faisal, Selen, & Wolpert, 2008). For example, sensory data is merely the result of firing peripheral receptors and not a direct measurement of the parameter of interest (e.g. joint angles, limb position, velocity etc.) (Bays & Wolpert, 2007). Also, the numerous DOF combined with inherent dynamics in the body and environment ensure that no motor plan is ever duplicated in exactness. Consequently, each movement is accompanied by a unique dataset of resultant sensory information. As follows, the estimation of the current state of the body cannot be as simple as 'a + b = c'. Rather, the CNS must infer the most likely body state from uncertain sensory evidence and use it to inform the execution of a motor plan that most effectively meets the task demands. Accordingly, the more accurate and up-to-date that incoming sensory information from a body part is, the more accurate the resultant estimate for the state of that body part will be. Taken further, a person with a sensory system that delivers richer information at a faster rate will perceive bodily states with greater fidelity than a person with less clear and slower sensory information. Ultimately, a person with cleaner sensory data (e.g., less noisy) has a greater chance of correctly executing an appropriate movement than a person with damaged sensory data. Because of this, acquiring and processing accurate sensory information is imperative towards successful movement.

Sensory acquisition

Sensory acquisition involves the passive process by which sensory data is obtained from peripheral receptors and relayed to various areas of the CNS to be further processed. In its most elementary form, somatosensory information results from specific stimuli activating sensory receptors embedded on and within the skin, joints, tendons, and muscles. The exact information that each sensory nerve cell carries is dependent upon the type of sensory receptor it is associated with. Muscle spindles, located within skeletal muscle, communicate changes in muscle length and the speed of lengthening (Hulliger, 1984). Golgi tendon organs located at the junction between muscle and tendon detect muscle forces (Crago, Houk, & Rymer, 1982). Joint receptors found in the connective tissue surrounding joints detect limits to range of motion (Proske & Gandevia, 2009). Cutaneous receptors in the skin detect pressure, vibration, and discriminative touch. The following section will detail how and why the process of acquiring sensory data and transporting it back to the CNS for analysis is an integral component of the nervous systems' ability to move the body.

Signal strength

In research, scientists labor to ensure the data they collect is truly reflective of the scientific questions involved in the study. When designing a research experiments, elaborate procedures are often put in place to decrease the chance of tainted data and to maximize the chance of representing the true parameter(s) of interest. Researchers understand that the quality of data collected determines the conclusions that can be drawn from a specific dataset. This idea is formalized by the data-processing inequality theorem that states that for any stage in data processing, the amount of information that can be extracted is limited to the efficacy of earlier stages (Cover & Thomas, 2006; Faisal et al., 2008). For the same reasons, the quality of sensory information that is acquired by receptors in the periphery greatly influences the perceptual capabilities of the CNS during later stages of processing. Interestingly, many structural and functional characteristics of the human nervous system help to ensure the accuracy of sensory information relayed to the CNS. This is made evident in both the quality and quantity of sensory data collected at the periphery.

Sensory Data Quality

In the human body, the delegation of energy sources can be used to understand which physiological processes are of priority when ensuring the overall health of the organism. For example, the human brain requires roughly twenty percent of the overall metabolic budget of the body even though it makes up approximately two percent of the overall body mass (Sokoloff, 1960). However, due to the essential role that brain function plays in overall health, this metabolic investment is supported by the energetic system. Within this metabolic budget, the majority of neural energy resources are dedicated to neural signaling(Rothman et al., 1999). As follows, in most neurons within the CNS, energy producing mitochondria are strategically located near the nodes of Ranvier to provide adequate energy to the sodium potassium pump and assist in fast propagation of the action potential along the axon (Chiu, 2011; Ohno et al., 2011). However, in contrast to neurons in the CNS, the area of greatest mitochondrial density in peripheral sensory nerves is the distal synaptic junction to assist in efficient activation of the sensory nerve ending (Devine & Kittler, 2018; Kruger, Light, & Schweizer, 2003; Sajic et al., 2013). This finding suggests that, in contrast to maximizing the signal speed as is the case for most CNS neurons, peripheral sensory nerves maximize the proper function of the sensory nerve ending to respond to appropriate stimuli. In this case, the energetic system provides the ATP needed to transport mitochondria to the distal end of sensory nerves as well as the resultant ATP that is generated by the mitochondria to ensure the acquisition of quality sensory information.

Sensory Data Quantity

In many scenarios when designing a research experiment, it is commonly understood that a larger sample size is advantageous towards estimating the true test parameter. In a similar vein, by combining the sensory information from multiple sensory types, it provides a more accurate understanding for where the body parts are as they execute different motor tasks. Furthermore, it is believed that the human upper limb contains roughly 4,000 muscle spindles, each containing multiple afferent axons, 2,500 Golgi tendon organs, a few hundred joint receptors and almost 20,000 myelinated cutaneous receptors solely located on the surface of the hand (Hulliger, 1984; Johansson & Vallbo, 1979; A. Prochazka, Westerman, & Ziccone, 1977). In a recent finding, Gesslbauer and colleagues (2017) examined the human brachial plexus, the neural bundle containing all nerve cells responsible for controlling arm and hand movements. The authors discovered that of the almost 350,000 axons found in the brachial plexus, ninety-three percent were sensory axons leaving the remaining seven percent to communicate the motor information needed to control arm and hand movements. Thus, by collecting multi-faceted sensory data from numerous locations throughout the involved limbs and joints, the CNS gains the greatest insight on the true state of the body. In combination with the energetic evidence illustrating the priority placed on the acquisition of quality sensory information, the structure of the peripheral nervous system further implies the importance of the amount of sensory data available to the CNS in the control of movement.

Signal Speed

Once somatosensory information has been acquired from peripheral sensors, it must be transported to the CNS in a manner that maximizes signal integrity and time efficiency. Because there is an inherent delay between sensory stimulus and CNS perception, the accuracy of the state prediction is limited by the speed at which the sensory information becomes available to the CNS. Many movements, such as gait and balance, require near instantaneous access to sensory information to avoid harmful errors and ensure goal attainment. Accordingly, the CNS is structured in a way to bring this essential sensory information to the brain as fast as possible. Once the adequate sensory stimulus has elicited the firing of a primary afferent nerve ending, neurons carrying proprioceptive information (muscle spindles, Golgi tendon organs and joint receptors) travel to the brain via group Ia afferent axons. This fact is important because these axons are the most myelinated axons in the CNS (Steffens, Dibaj, & Schomburg, 2012). This heavy myelination maximizes the maintenance of signal quality and enables a conduction velocity among the fastest in the nervous system and, interestingly, faster than their efferent counterparts (Steffens et al., 2012). Furthermore, the group Ia axons carrying proprioceptive information specifically to the cerebellum yield the fastest conduction velocity within the CNS (Edgley & Gallimore, 1988). The heavy myelination of proprioceptive axons allows this crucial information to reach the brain faster than sensory information from vision notwithstanding the greater conduction length (Cluff, Crevecoeur, & Scott, 2015). As a result, goal-directed motor responses to somatosensory feedback can be generated roughly 30 ms faster than goal-directed motor responses from visual feedback (Dimitriou, Wolpert, & Franklin, 2013; Jin, Wang, Lashgari, Swadlow, & Alonso, 2011; Scott, 2016).

Fast access to somatosensory information comes at a high energetic price. Laughlin and colleagues estimated the energetic cost of acquiring and transporting sensory information from the eye to the CNS to be 7 x 106 molecules of ATP per bit of sensory information (Laughlin, van Steveninck, & Anderson, 1998). Furthermore, this cost increases with distance from the CNS as well as the priority placed on a specific sensory type. Thus, it is likely that the metabolic cost of somatosensory information from the upper and lower extremities far surpasses Laughlin's estimate. For this cause, it has been suggested that the heavy myelination of peripheral axons is a central mechanism put in place to decrease the metabolic cost of transporting sensory information (Harris & Attwell, 2012). However, when including the energy required by the oligodendrocytes and Schwann cells to myelinate group Ia axons into the calculation, Harris and Attwell discovered that the energy saved in signal transportation is insufficient to compensate for the energy spent to myelinate these sensory axons (Harris & Attwell, 2012). Therefore, it is likely that the main role of this heavy myelination is solely to increase propagation speed rather than reduce the energy consumption of signal transportation. As follows, the metabolic system allots the vast amount of ATP required to myelinate group Ia afferent axons (as plentiful as they are) to ensure the fast communication of sensory information from the skin, muscles and joints to the brain.

Injury, disease and aging often negatively impact the availability of sensory information for the CNS to use when controlling movements (Cameron, Horak, Herndon, & Bourdette, 2008; van Hedel & Dietz, 2004; Vidoni & Boyd, 2009; York, Perell-Gerson, Barr, Durham, & Roper, 2009). An example of impairments caused by diminished sensory acquisition is sensory neuropathy caused by diabetes. The most common symptom of diabetes is sensory nerve cell death in the periphery (Albers & Pop-Busui, 2014; Yagihashi, Mizukami, & Sugimoto, 2011). This damage causes decreased sensation in the periphery hindering the ability to sense movement errors leading to further injury. York and colleagues (York et al., 2009) sought to teach diabetic patients an altered gait pattern that would decrease the prevalence of foot ulcerations. However, in contrast to healthy controls, patients were unable to retain the new skill. A likely contributor to this inability to learn a new movement is because they could not collect sufficient sensory information indicating movement errors/successes. Additionally, multiple sclerosis is a chronic neurodegenerative disease that impairs the quality of white matter within the CNS. The harm to myelin impairs the quality of neural signaling leading to many motor impairments such as impaired balance and fall risk (Sosnoff et al., 2011). Cameron et al. (2008) discovered that the leading cause of balance impairments in people with multiple sclerosis is slowed conduction velocity of somatosensory information through the spinal cord. Thus, a prominent cause for mobility decrements in this population is due to an inability to access their sensory information fast enough to form an accurate estimate of the state of the limb/body part. Additionally, research in patients with decreased proprioception due to stroke, aging, or spinal cord injury has shown that the ability for these populations to learn locomotor tasks is governed by their remaining proprioceptive ability (Chisholm, Qaiser, Williams, Eginyan, & Lam, 2019; van Hedel & Dietz, 2004; Vidoni & Boyd, 2009).

In summary, because of its large impact on successful movement, great priority is placed on acquiring and transporting somatosensory information to areas where it will be further processed. This is made evident in various mechanisms put in place to ensure a large amount of quality sensory information is acquired from somatosensory receptors throughout the body and transported to the brain as fast as possible. This assists the CNS in calculating an accurate and up-to-date perception for the current state of the body as its various parts perform goal-oriented movements.

Sensory processing

When somatosensory data arrives at supraspinal regions to be further processed, there are inherent challenges that the CNS must address to use the incoming data to assist in movement control. First, the received input, in its raw form, is merely an assemblage of electric signals communicating a change in somatosensory stimuli. To be processed into a perception of bodily state, the incoming data must be given meaning in the greater context of the body and environment. Next, although proprioceptive information arrives with the shortest temporal delay, some degree of a delay is inevitable. Thus, the CNS must address this delay to coordinate movements with smoothness and precision.

In this section, I highlight three essential neural processes that assist the CNS with these inherent challenges. By understanding these crucial processes, we can gain important insight into the role that somatosensory information plays in movement control and better identify areas that can be improved through rehabilitation and intervention. First, I identify the need for accurate sensory predictions to give meaning to incoming sensory stimuli. Afterwards, I review how the incoming sensory information is combined with sensory predictions to calculate the most optimal estimate of the current bodily state that decreases the harmful effects of variability. Finally, I discuss how sensory information contributes to identifying a movement strategy that ensures the optimal performance of a motor skill. I begin each section by explaining each specific processing step and then provide examples that demonstrate their importance. Throughout this section, I rely on theoretical and empirical research from multiple populations to demonstrate the importance of sensory processing in the overall control of movement.

Sensory Prediction

When sensory information arrives at supraspinal areas for further processing, it is relayed to multiple areas to inform the brain on the current state of the body parts involved in a motor task. However, because the brain does not have direct access to the parameter of interest (e.g. joint angle, limb position etc.), it is difficult to perceive the state of the body based off noisy afferent signals. Much research over the last twenty years suggests that the brain addresses this challenge by comparing the incoming sensory information to a prediction that is heavily influenced by the sensory data obtained from previous movement attempts (McNamee & Wolpert, 2019; Miall & Wolpert, 1996; Wolpert, Miall, & Kawato, 1998). By retaining this sensory data, the brain can construct forward models that simulate the physical and sensory outcomes of ensuing motor commands of a similar type. Thus, with every motor command there is an expected sensory consequence that is used to determine movement accuracy when the actual sensory information becomes available.

Discrepancies between the predicted consequences and the actual sensory data are used to improve the forward model for ensuing movement attempts to minimize discrepancies in the future. However, this is only possible when the CNS reliably understands the motor system to the point that the sensory predictions are in line with the actual sensory consequences. Flanagan and colleagues (2003) showed that when learning a novel motor task, participants learned the appropriate sensory consequences much faster than they learned the motor commands necessary to perform the task reliably. Along those lines, there is ample evidence to show that structural and functional changes to sensory areas of the brain accompany improvements in motor skill performance in healthy and clinical populations (Gaser & Schlaug, 2003; Sehm et al., 2014; Sidarta, Vahdat, Bernardi, & Ostry, 2016). But, Ohashi and colleagues used electroencephalography (EEG) and somatosensory evoked potentials (SEP) to show that plasticity in the somatosensory areas of the cortex precede those seen in motor areas while learning a novel motor skill (Ohashi, Gribble, & Ostry, 2019). Accordingly, a firm understanding of what a movement should feel like is indicative of the state of the body and essential toward the effective performance of that movement.

The importance of accurate sensory predictions is evident in both healthy and clinical populations. A person whose incoming sensory information is more representative of the true state of the associated body part can construct forward models that more reliably predict the sensory consequences of a certain motor command. When describing athletic performance, Yarrow and colleagues described elite athletes as ‘people who have learnt very good forward models at various levels of representation allowing them to plan better movements in any context.’ In contrast, aging results in impairments in the sensory system which hinder one’s ability to form accurate forward models (Boisgontier & Nougier, 2013). As a result, their understanding of the consequences of motor commands decreases along with the amount of body states they can reliably perceive (Boisgontier & Nougier, 2013; Ghafouri & Lestienne, 2000; Lafargue, Noel, & Luyat, 2013). Additionally, Smith and Shadmehr (2005) showed that patients with cerebellar degeneration were unable to learn from previous movement attempts and accurately predict movement consequences. This inability leads to deficits in movements of both the upper and lower extremities (Fonteyn et al., 2010; Topka, Konczak, Schneider, Boose, & Dichgans, 1998). Furthermore, research in other clinical populations has shown that a disruption in one's ability to accurately predict sensory consequences plays a very large role on their ability to move correctly (Arpin et al., 2017; Shaffer & Harrison, 2007; Smith & Shadmehr, 2005).

Anatomically, the process of comparing incoming afferent information to sensory predictions to form a perception of the body state involves multiple neural structures throughout the brain. However, much research suggests that the sensorimotor cortices and the cerebellum are heavily involved (Bastian, 2006; Blakemore, Frith, & Wolpert, 2001; Ishikawa, Tomatsu, Izawa, & Kakei, 2016; Kumar, Manning, & Ostry, 2019; Makino, Hwang, Hedrick, & Komiyama, 2016; Miall & Wolpert, 1996; Wolpert et al., 1998). It is well established that the cerebellum is the location that afferent sensory information is compared to sensory predictions (Blakemore et al., 2001; Cullen & Brooks, 2015; Wolpert et al., 1998) however, whether those sensory predictions are stored within the cerebellum is unknown. In a recent review, Ishikawa et al. (2016) provide evidence that the cerebro-cerebellum is the location of these sensory predictions. Yet, Galea used transcranial direct current stimulation (tDCS) to show that the cerebellum is involved with learning from prediction errors and improving subsequent attempts but the retention of sensory predictions are stored within the cortex (Galea, Vazquez, Pasricha, de Xivry, & Celnik, 2011). Kumar and colleagues (2019) also identified the cortex as the area that sensory predictions may reside. Details of the neural resources required to form sensory predictions should be the focus of future research. In conclusion, somatosensory information is not only beneficial for the current movement but also greatly improves the efficacy of future attempts by contributing to predictive forward models.

State Estimation

Sensory predictions assist the CNS in calculating the current state of the body while performing different motor tasks. However, due to the ambiguity and variable nature of sensory information, some degree of uncertainty remains in this neural calculation. Additionally, the challenge of calculating the current state from delayed sensory information remains. A growing body of research suggests that the CNS addresses both the uncertainty of sensory data and the temporal delay in a way consistent with a statistical model known as Bayesian inference (Kording & Wolpert, 2004a, 2006; Shadmehr & Krakauer, 2008; Wolpert, 2007).

Bayesian Inference

Prior to elaborating on how Bayesian inference is used to understand sensory uncertainty in motor control, I will provide a brief explanation of this model and the variables involved in its use. Bayesian inference stems from a statistical model of probability known as Bayes' theorem developed by Thomas Bayes in 1763 (Figure 1.1).

$$P(A|B) = \frac{P(B|A) * P(A)}{P(B)}$$

$P(A|B)$ = The Posterior. The probability of "A" being true, given "B" is true.

$P(B|A)$ = The Likelihood. The probability of "B" being true, given "A" is true.

$P(A)$ = The Prior. The probability of "A" being true.

$P(B)$ = Marginalization. The probability of "B" being true.

Figure 1.1. Bayes theorem of probability.

Bayesian inference is a method of statistical inference that uses Bayes' theorem to calculate the most probable estimate for an unknown parameter by considering multiple sources of information.

The first source of data considered in Bayesian inference is the likelihood distribution. The likelihood is a function of the available evidence and can be interpreted as the probability of observing a value x given that x is equal to the unknown parameter. Figure 1.2 provides an illustration of Bayesian inference with simulated data. In figure 1.2, the likelihood distribution is displayed in yellow and generated from a dataset with a mean equal to fifteen and a standard deviation equal to either two or four. The second source of information included in Bayesian inference is the prior distribution and can be described as the probability of a given value x being equal to the unknown parameter

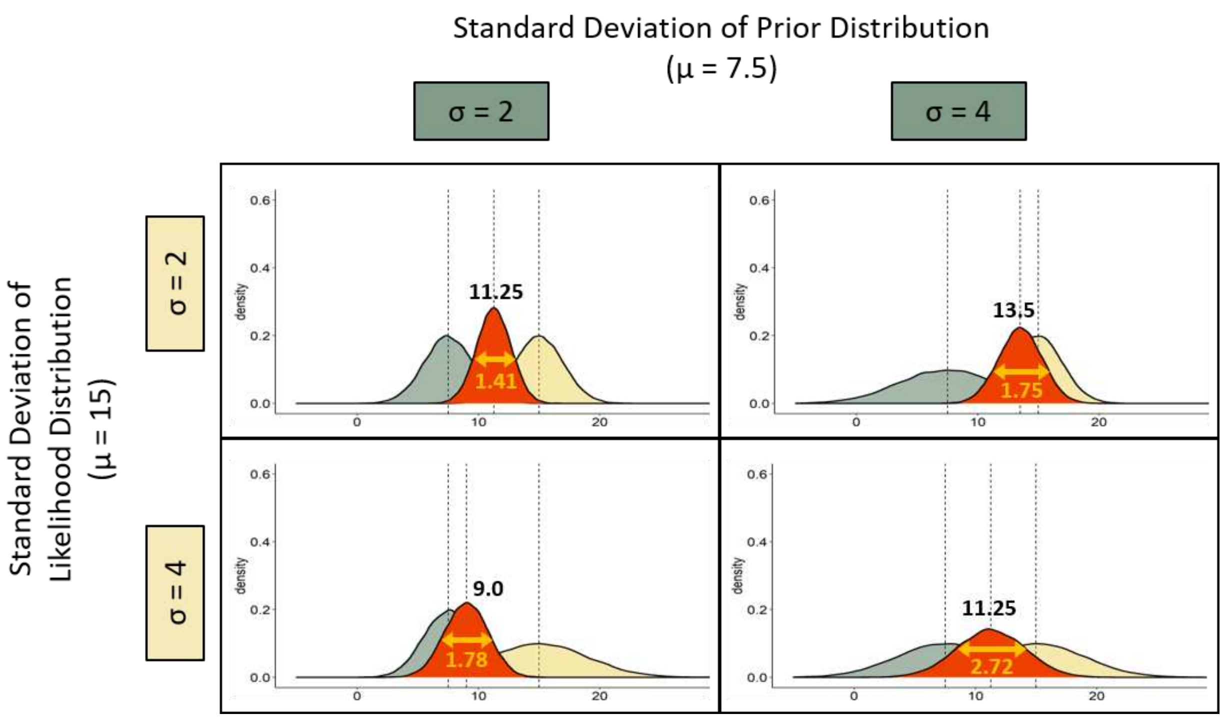


Figure 1.2. The resultant posterior distribution (orange) under various characteristics of the prior (green) and likelihood (yellow) distributions. The posterior distribution is proportional to the likelihood distribution times the prior distribution

without considering any of the recent evidence. In Bayesian inference, the prior distribution is often changing as new data is collected and is stored, in a way, to inform the interpretation of future datasets. In figure 1.2, the prior distribution is represented in green and was generated from a dataset with a mean equal to either two or four.

Bayesian inference relies on the posterior distribution to provide the most likely estimate of the unknown parameter considering both the likelihood and prior distributions. The posterior distribution is proportional to the likelihood distribution times the prior distribution and is described as the probability of the unknown variable being equal to x given that x is the observed value. The characteristics of the posterior distribution, represented in orange in figure 1.2, are determined by the means and standard deviations of the prior and likelihood distributions. By considering both the prior and the likelihood distributions, the variability of the posterior distribution is minimized to a value smaller than either of those sources of information taken in isolation, maximizing the likelihood of estimating a value nearest to the unknown parameter.

When applied to sensorimotor control, Bayesian inference is used to estimate the unknown state of a given body part. In the Bayesian inference context, the most likely estimate for the location of a body part is calculated by considering the mean and variability of both the recent sensory information as well as the expected location of the body part despite the current sensory data. As mentioned earlier in the Introduction, sensory information is ambiguous, and the same sensory data can represent many possible states of a given body part. For this purpose, the likelihood is represented by the incoming sensory information. While it is true that a certain set of sensory information can represent multiple bodily states, not all possible body states are equally probable.

Additionally, body states that are more probable result in sensory information that is less variable. In the Bayesian framework, the prior distribution represents the most likely body states based on previous experiences performing similar movements. According to the Bayesian model of motor control, the posterior distribution is calculated by the CNS and is proportional to the likelihood distribution (sensory data) times the prior distribution (most likely body states). By allowing the most probable body states to influence the estimation of the actual body state, the CNS increases the probability of making an accurate estimate. Additionally, by combining the most recent sensory data, albeit temporally outdated, with the predicted bodily state, the CNS can form the optimal estimate for the immediate body state. For example, if the CNS is controlling a new movement, the expected bodily state and associated sensory prediction are unsure and thus, quite variable. As a result, more weight will be placed on incoming somatosensory data to estimate the body's location. On the other hand, if a motor skill is well learned, the sensory predictions and expected bodily states are quite precise and will greatly influence the final estimate when incoming sensory data is compromised such as when walking after taking an ice bath.

Many factors impact the quality of sensory information that the CNS uses to calculate the likelihood distribution. Age, health status, previous movement history and fatigue level (among others) all can influence the variability that accompanies the sensory data collected by peripheral receptors. Due to the iterative nature of the prior distribution, this sensory variability also impacts the uncertainty included in the prior distribution. A young healthy athlete with superior sensory acuity of the peripheral receptors would theoretically have less variability in their likelihood distribution which would then inform a more certain prior distribution after many attempts of the movement. In the same context, an elderly gentleman with peripheral neuropathy would likely have more variability in their likelihood distribution of sensory data and also have a wider spread of the prior distribution. As follows, the young athlete would likely make a more accurate estimate of body position with less uncertainty than the elderly gentleman Figure 1.3).

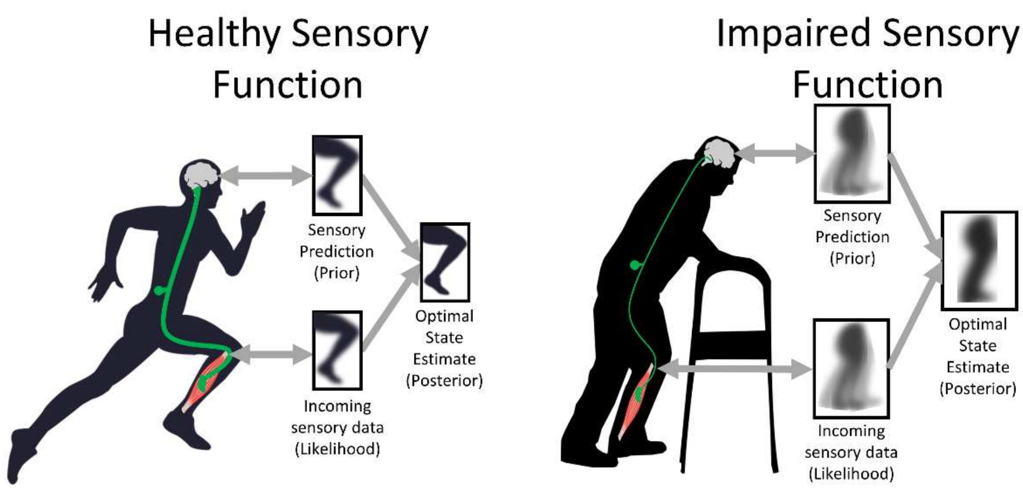


Figure 1.3. Optimal estimation of the state of a limb comes when considering both the incoming sensory information as well as the sensory prediction based on previous experiences in the movement space. An individual with better sensory function will form state estimates with greater fidelity to the actual state than an individual with an impaired sensory system.

Anatomically, Ishikawa et al. suggest the neural location where incoming sensory information is compared to expected sensory predictions is at the granule cells of the cerebellum (Ishikawa et al., 2016). The granule cells receive projections from the cortex as well as incoming sensory information via the spinocerebellar tracts. This suggestion is particularly interesting because over half of the energetic budget of the cerebellum is dedicated to the granule cells, further suggesting the prioritization of acquisition and processing of sensory information to control movement (Howarth, Gleeson, & Attwell, 2012). While the comparison of expected and actual sensory data appears to occur in the cerebellum, neural markers of uncertainty appear to reside in other regions. Tan and colleagues have shown consistently that the cortico-basal network is heavily involved in the indexing of confidence in expected sensory data and bodily states (Tan, Jenkinson, & Brown, 2014; Tan, Wade, & Brown, 2016; Tan, Zavala, et al., 2014; Zavala et al., 2016). Evidence shows that synchronization in the beta oscillations (measured with EEG) over the sensorimotor cortices is responsible for indexing the confidence one has in their sensory predictions following the completion of a motor skill (Tan et al., 2016). An increase in beta power (synchronization) over the sensorimotor cortex at the end of a movement signifies a strong agreement between the expected and actual sensory datasets. This post movement beta synchronization (PMBS) decreases with sensory prediction errors that signify low confidence in sensory predictions and high uncertainty. A decrease in PMBS has been interpreted as the CNS updating the current model to assist with future attempts (Tan et al., 2016). Arpin et al. (2017) reported decreased PMBS in individuals with MS and showed that better motor performance correlated with greater PMBS indicating those with better performance maintain accurate state estimations. Similar work has shown that patients with sensory deafferentation report a decreased PMBS following performance of a fine motor task (Reyns, Houdayer, Bourriez, Blond, & Derambure, 2008). Interestingly, evidence shows that the PMBS is driven by the subthalamic nucleus, a crucial region of the basal ganglia that influences the activity of the indirect pathway (Tan, Zavala, et al., 2014). Thus, it is possible that by means of manipulating the balance between the direct and indirect pathway of the basal ganglia, the CNS indexes the confidence to be placed on sensory information or prior expectations when controlling for the noise inherent to sensory information. In summary, the unification of incoming sensory information with expected sensory and bodily states enables the CNS to make the most accurate estimate for the actual body state. In a way consistent with Bayesian inference, the CNS can make these estimations throughout the completion of motor tasks minimizing the effects of uncertainty and time delay that accompany sensorimotor control. In all areas of these neural processes, sensory information that is more accurate, and less variable will lead to greater performance in goal-oriented movements.

Movement Optimization

Whether reaching for a glass of water, walking around the neighborhood, or dribbling a basketball, each movement has a desired outcome that the CNS achieves through the contraction of muscle. To this point, emphasis has been placed on monitoring the incoming sensory information to form the most accurate estimate for the state of the limb as it accomplishes the specific goal of the movement. However, in most cases it is not enough to simply achieve the movement goal. For example, if a ball is flying towards one's face, the movement goal is to move a hand to the appropriate place to intercept the incoming ball. Undoubtedly, there are multiple ways to move the hand from its current location toward the face, but the ideal movement ensures that the hand will arrive in time to catch the oncoming ball and avoid injury. Such a quick movement would involve energetically expensive contraction of muscles and other affiliated costs. However, it would avoid the harmful effects of the ball striking the face. Thus, for every movement there is an overarching goal that is accompanied by an associated reward and cost, which vary depending on the movement context. As a result, the optimal movement is often one that maximizes the chance of reward and decreases the associated cost of the movement. Still, due to the complexity of the system and the accompanying variability, movement errors are unavoidable. However, not all errors are created equal in the greater context of the movement goal. In the context of the previous example, an error that resulted in the hand intercepting the ball one inch closer to the face than expected is more acceptable than the hand being one inch too low and missing the ball altogether. Thus, the optimal movement is one that maximizes the reward of a movement and decrease the affiliated cost by avoiding errors that are detrimental towards the movement goal and tolerating unrelated errors. This model of how voluntary movements are controlled is known as optimal feedback control (OFC) and reliably explains the use of sensory information during movements (Krakauer & Mazzoni, 2011; Scott, 2004, 2012; Shadmehr & Krakauer, 2008; Shadmehr, Smith, & Krakauer, 2010; Todorov, 2004; Todorov & Jordan, 2002). OFC emphasizes that the outcome of the movement is what matters and not the specific characteristics of the movements themselves.

The process of identifying the sensory information that is most pertinent to the outcome of the movement involves multiple experiences learning the input-output relationships of the body parts involved. By so doing, the CNS is able to observe the associated reward of a movement and retroactively give credit (or blame) to the sensory data that accompanied it (Wolpert, Diedrichsen, & Flanagan, 2011). This process of using reward values to fine-tune motor output is known as reinforcement learning and has been shown to largely be governed by the basal ganglia (Doya, 1999; Ito & Doya, 2011). In reinforcement learning, the basal ganglia (and other regions by a lesser degree) use dopaminergic projections to give associated reward values to each movement. Accordingly, with great amounts of experience in the movement space, the CNS can calculate an expected reward for each possible movement. As a result, each motor command sent from the CNS involves a set of sensory predictions as well as the associated expectation of reward.

While controlling a movement, if there is a large sensory prediction error but the associated reward was minimal, there is no need to expend energetic resources to correct the error prone movement. However, if there is great variability in the incoming sensory information, there is also uncertainty in the associated value of the movement (Lak et al., 2020). Accordingly, sensory information that is accurate and temporally relevant is incredibly beneficial in identifying the optimal movement. Crevecoeur and colleagues (2016) provided evidence that proprioception has a larger contribution to optimal control than other sensory types due to its prompt availability to the CNS. In this sense, quality sensory information not only contributes to an accurate estimate for the current state of the body parts involved in the movement, but it also assists with the identification/execution of movements more/less likely to result in rewarding movements. Accordingly, an individual who is better able to accurately estimate the state of their body and the associated value that accompanies it, is better able to achieve the movement goal in a way that optimizes the value of the movement.

Methods of Studying Somatosensation in Motor Control

Thanks to the drove of research discussed above, we know that sensory information is important to successful motor performance. This reformed viewpoint on sensory function has sparked a desire by many interested researchers and practitioners to administer methods of sensory assessment to the research participants, patients, and athletes that they interact with. However, agreeing upon ideal methods of assessing sensory function in motor control has proven to be difficult for investigators participating in this area of research. A large reason for this lack of agreement is due to the multi-faceted nature of how sensory information is used to control movement. One of the most impactful conclusions that can be drawn from this renewed appreciation for sensory information in movement is that it is much more nuanced than previous attempts to reduce it to "body position sense" or "muscle sense." It is not the purpose of this section to provide an exhaustive list of the sensory mechanisms involved in motor control or all methods used to study and assess somatosensation. For reviews of this nature, refer to (Aman, Elangovan, Yeh, & Konczak, 2014; Elangovan, Herrmann, & Konczak, 2014; Han, Waddington, Adams, Anson, & Liu, 2016b; Arthur Prochazka, 2021; Proske & Gandevia, 2009). Rather, I intend to discuss a few of the nuances involved with assessing sensory function in motor control to emphasize a need for careful planning and purposeful study design when seeking to assess or investigate these important neural processes.

In many scenarios, sensory information from the muscles, joints and connective tissue is referred to as "proprioception." This term was first used by Sir Charles Sherrington and referred to as "the perception of joint and body movement as well as position of the body, or body segments, in space" (Sherrington, 1906). Since Sherrington's first definition, many subsequent definitions have been attempted and used to explain sensory function as it pertains to motor control. In many cases, proprioception is meant to refer to neurophysiological processes such as the function of mechanoreceptors in the periphery

(Sokhangu, Rahnama, Etemadifar, Rafeii, & Saberi, 2021), the quality of neural pathways (Fling, Dutta, Schlueter, Cameron, & Horak, 2014), or the function and communication of cortical regions (Goble, 2010). In other contexts, proprioception is used to describe the raw ability to sense limb position or motion without the use of vision (Elangovan et al., 2014; Goble, 2010). Furthermore, proprioception is often referred to as a broader sense of body awareness while motor skills are being performed (Han, Anson, Waddington, & Adams, 2014; Han, Waddington, Adams, Anson, & Liu, 2016a).

To remove some of the confusion regarding the interpretation of proprioception, the term "kinesthesia" has been used to refer to the conscious perception of body position and movement and reserve "proprioception" for referring to the unconscious processes involving body position information (Elangovan et al., 2014; Arthur Prochazka, 2021; Proske & Gandevia, 2009). However, this distinction is not universally acknowledged as "kinesthesia" and "proprioception" are often used interchangeably (Han et al., 2016a), or used to delineate motion sense and position sense, respectively (Aman et al., 2014). Regardless of how the terms are defined, proprioception is clearly more than simply the firing of mechanoreceptors in the periphery, and we must avoid "the fallacy of ascribing proprioception to proprioceptors", as James Gibson argued in 1966 (Gibson, 1966). For the purpose of this Introduction, I'm merely striving to highlight the importance of somatosensory information in skilled motor performance and thus, no distinction or preference for one view over the other shall be expressed. Rather, I aim to emphasize the need for careful consideration when seeking to conduct or interpret research focusing on proprioception and related topics.

Neurophysiology and Anatomy

A large component of how somatosensation impacts motor performance is the function and anatomy of the neurophysiological processes involved in acquiring and processing the incoming sensory data. There are multiple methods available to investigate these crucial neural processes that must be chosen depending on the specific questions of a research study. As mentioned previously, muscle spindles are found within each muscle and report crucial information regarding length and rate of muscle stretch. A common way to assess these key sensory receptors is to impose a muscle stretch and measure the reflexive response. The simplest way this is done is to impose a rapid stretch by tapping a tendon with a tendon hammer which rapidly elongates the muscles and evokes a burst of activity in the afferent muscle spindles responding in an activation of that same muscle through monosynaptic reflex mechanisms (Dick, 2003). In addition, one might be interested in the resultant cortical processes that are recruited to process and integrate sensory information that results from movement. Once again, there are multiple ways to investigate these mechanisms. When a burst of afferent information is received by the CNS (such as the resultant activity of the tendon tap assessment discussed above), a sensory evoked potential (SEP) can be measured at the level of the cortex using either electroencephalography (EEG) or magnetoencephalography (MEG) (Illman et al., 2020; Ohashi et al., 2019; Seiss et al., 2002). These methods enable immediate measurement of the neural resources utilized to process incoming sensory data. However, although EEG and MEG provide superior temporal precision, they lack spatial precision to identify specific regions of activity resulting from afferent information. Additionally, both methods require many apical dendrites aligned in parallel close to the skull surface to be able to measure the underlying neural activity. For spatial resolution or subcortical activity, functional magnetic resonance imaging (fMRI) is often used to locate highly specific regions of the brain that are involved with sensory processing, though fMRI lacks the temporal precision characteristic of EEG/MEG data (Iandolo et al., 2018). In addition to these methods, transcranial magnetic stimulation (TMS) methods are often utilized to identify neurophysiological properties or levels of neural excitability that allow sensory integration and motor learning (Mirdamadi & Block, 2020; Ohashi et al., 2019).

Proprioceptive Assessments

While neurophysiological and anatomical investigations are vital to understand sensory function, many clinicians and practitioners do not have access to the equipment mentioned above, nor are they interested in the results that they provide. Rather, they are often interested in the raw ability to detect and sense body position (with the assumption that it is informed by functioning mechanoreceptors mentioned above). Many clinical assessments have been used to measure proprioception in various contexts. One method commonly used is the threshold to detect passive motion test (TTDPM). In this method, the investigator will move isolated body segments (either manually or with a machine) in a predetermined direction while other peripheral information is occluded, usually by blindfolds or headphones, etc. Participants are instructed to push a button or verbally respond as soon as they perceive the movement and direction (Han et al., 2016a; Refshauge, Chan, Taylor, & McCloskey, 1995). Gibson (1966) labeled this type of proprioceptive information as "imposed proprioception" as it results entirely from external manipulation. For this purpose, Elangovan et al. (2014) refer to this method as the "purest" possible measure of proprioceptive function. In contrast, Han and colleagues

(2016b) argue that this method of assessing proprioceptive function lacks ecological validity because few daily movements involve passively imposed movements. Also, Gandevia et al. (1992) suggest that muscle spindle activity is diminished in passive movements and, as a result, the TTDPM test is largely measuring only the function of cutaneous receptors.

Alternatively, the joint position matching (JPM) test has been used to incorporate self-generated movement in the assessment of proprioception. In this assessment, individuals are asked to replicate a reference joint position without the assistance of vision (Elangovan et al., 2014; Goble, 2010). There are two variations of this task that are generally used to assess proprioceptive acuity in clinical populations. In the contralateral JPM task, the opposite limb is passively moved to a target joint angle and participants are asked to concurrently match the target joint angle with their opposite limb. The difference in joint angle between the two limbs has been used as a quantitative mark of proprioceptive acuity in that specific limb and joint (Goble, 2010). In the ipsilateral JPM task, the participant’s limb is passively moved to a target joint position and then returned to a base position. Participants are then asked to re-create the target joint angle with the same limb. Like the contralateral task, the difference between the reference and matching joint angles is used to measure proprioceptive function. While the JPM does involve active movement in its assessment of proprioception, it is not without limitations. In all variations of this assessment, the individual is required to compare two different sensory signals and identify the point where they are identical. In the contralateral JPM task, this is often done while comparing the sensory signals from both limbs simultaneously. However, the reference limb is usually moved to its position passively by the investigator and the matching limb must be actively moved by the participant. As mentioned above, the sensory consequences of passive versus active movements are different and thus, it introduces a degree of error as participants are required to match the same joint angle. In the ipsilateral JPM task, participants must maintain the sensory signal of the reference limb in memory as they reproduce the exact limb position with the same limb (either actively or passively). In this scenario, a degree of error is introduced as participants' short-term memory will play a large role on their ability to match the two sensory signals. While both methods of assessment (TTDPM and JPM) are useful for specific aspects of proprioceptive function, investigators need be aware of the differences in neural processes that are being assessed. Especially because research has shown that performance in these two types of tests is not correlated when measured from the same ankle (Jong, Kilbreath, Refshauge, & Adams, 2005).

Behavior

I have discussed ad nauseum the levels of complexity that are associated with skilled motor performance in daily lives, in athletic competition, and other realms of human performance. Thus far I have highlighted many ways that somatosensation permits the motor behavior observed in many of these areas. A large reason for the ambiguity and lack of agreement in what proprioception is and how its assessed is because, by in large, our understanding of it can only be inferred from human behavior. Clearly the neurophysiology and anatomical systems that gather and process the information are vital, but it is always behavior that we most want to understand and improve. Again, I refer to the early definition of proprioception by Sherrington as "the perception of joint and body movement as well as position of the body, or body segments, in space." As we endeavor to study and assess proprioception, we must remember that we are chasing a perception that is built upon sensory information and demonstrated through skilled behavior. This approach to assessing sensorimotor control, known as psychophysics, refers to the quantitative investigation of the relationship between an objective stimulus and the subjective perceptions that it causes (Han et al., 2016b; Schmidt, 1991). Sensory information is inherently uncertain and clouded with variability and, as a result, the CNS must form an estimate for the perceived state of each limb and joint. By using behavior to inform our understanding of this neural perception, we also must make an estimate for the function of one's somatosensory/proprioceptive system. We, as researchers, practitioners or clinicians are attempting to make an estimate of the estimate made by the CNS in perceiving body position. Due to this inherent limitation to the study of these sensory systems, vigilant intention must be given to identify the proper methods utilized to glean the desired data regarding a study design or assessment purpose.

The aim of cognitive neuroscience is to understand, through experimental investigation, the mechanisms that give rise to intelligent behavior (Waskom, Okazawa, & Kiani, 2019). In many regards, this aim is shared in the realm of sensorimotor control. The amount of insight that can be gained from the results of an assessment is dictated by the quality of experimental control that was put in place to produce the experimental results. When attempting to estimate the perception that results from sensory input, we must account for the inherent error present in both the estimate made by the CNS as well as our estimate gleaned from the experimental protocol. One method of controlling this inherent error is by controlling the amount of practice that is given for a given task prior to assessment. There is not an accepted amount of familiarization that is given for each test which leads to differing familiarization effects that may impact the overall score. Furthermore, these assessments generally involve only a few trials. When attempting to remove the uncertainty from one's prediction of sensory function, more trials are needed to more accurately reflect the actual distribution of sensory signal utilized by the CNS in perceiving body position. The increase in trials need also come with variability in task demands to minimize any learning effect as well as gain clearer insight into the ability of the CNS to form a perception of body position throughout a movement. Though these suggestions of controlled practice, increase in trials included and variability are contrary to current methods of sensory function in motor control, the resultant behavioral data will provide a clearer understanding of one's ability to utilize sensory input to perceive body state during skilled motor performance.

Conclusion

In conclusion, there are many different approaches and methods that provide data regarding the role of sensory information during motor performance. Depending on the specifics of the research question, one method is likely a better fit than others. As is the case in most scientific fields, the important thing is to carefully design an experiment or choose an assessment based on a specific and carefully formed research question. Similarly, it is also important to ensure the interpretation of the results gathered from an experiment or assessment are in line with the actual data that was gathered. As we continue to recognize that somatosensation and proprioception are much more nuanced than previously assumed, a vigilant attention to research and assessment methods will be vital towards increasing this understanding in the future.

Areas of intervention

In this introduction, I have provided evidence for the importance of collecting quality information from somatosensory nerves and explained various neural processes put in place to maximize the perception of our bodies as we perform movements, given the inherent variability in sensory data. Altogether, this evidence demonstrates that sensory information is essential in the control of movement and provides many areas that could potentially be exploited to improve human movement control. The following section will examine methods of intervention that approach movement training from a somatosensory perspective. These approaches, though relatively new, show promising evidence for improving motor function and ultimately to improve movement capabilities.

Electric stimulation

One method of improving movement through sensory interventions is with external electric stimulation. Nervous communication occurs via electric activity that can be modified in specific ways with the addition of external electric properties. The specifics of how nervous system communication is impacted is determined by the electric properties of the stimulation and where it is applied. This review will include examples from transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS) and transcutaneous electric nerve stimulation (TENS).

Transcranial direct current stimulation involves the passing of a low intensity electric current through the brain via electrodes placed on the scalp (Jacobson, Koslowsky, & Lavidor, 2012). This approach is relatively new and lacks consistent research findings. However, tDCS has received a lot of recent attention in the literature as a way to improve motor performance and has been included in this review because it will likely continue to be highly investigated because it is a relatively cost-effective method with potential for positive findings. The justification for this stimulation is to moderate the resting potential of the neurons in the area receiving the current. Recent work has shown that tDCS does indeed alter the cortical excitability of the brain (Minarik, Sauseng, Dunne, Berger, & Sterr, 2015). Cathodal tDCS raises the absolute resting potential, making it less likely for neurons to fire. Alternatively, anodal tDCS decreases the absolute resting potential of neurons making it more likely for neurons to fire. It is hypothesized that tDCS promotes neural plasticity through Hebbian processes that strengthen or weaken neural connections via an unsupervised learning framework. This type of neural adaptation occurs by strengthening synapses where the post-synaptic neuron consistently fires after the presynaptic neuron and weakening synapses that regularly fire in the opposite direction (Caligiore, Arbib, Miall, & Baldassarre, 2019; Doya, 2000). Azarpaikan et al. applied anodal tDCS over the cerebellum and parietal cortex as participants learned a novel bimanual coordination task (Azarpaikan, Taherii Torbati, Sohrabi, Boostani, & Ghoshuni, 2019). The authors showed that tDCS applied over the cerebellum and parietal cortices independently improved motor learning more than a group receiving no stimulation. Additionally, they showed that tDCS applied to the cerebellum was significantly more effective in improving motor learning than over the parietal cortex. These findings resonate with the role of the cerebellum in comparing the most recent sensory information with sensory predictions.

Most consistent findings applying tDCS over the parietal cortex come by applying cathodal stimulation to decrease the overall activity in this brain region (de Oliveira et al., 2019; Ishigaki, Imai, & Morioka, 2016; D. R. Young, P. J. Parikh, & C. S. Layne, 2020;

David R. Young, Pranav J. Parikh, & Charles S. Layne, 2020). This approach is often used with an investigative goal to identify the parietal cortex as a key brain region involved in proprioceptive processing and the internal representation of various motor tasks. Young and colleagues have shown consistently that cathodal tDCS over the posterior parietal cortex decreases the rate at which participants can adapt to various postural and gait perturbations (D. R. Young et al., 2020; David R. Young et al., 2020). These findings give hope that if anodal tDCS is used over the same region, participants may increase their rate of adaptation. However, this has not been consistently shown in the current literature when applied to motor skill performance (Doppelmayr, Pixa, & Steinberg, 2016; Pixa, Berger, Steinberg, & Doppelmayr, 2019), but body awareness and sensory integration has been shown to improve with anodal tDCS applied to the parietal cortex (Hirayama, Koga, Takahashi, & Osu, 2021; Hornburger, Nguemeni, Odorfer, & Zeller, 2019; Lira, Pantaleão, de Souza Ramos, & Boggio, 2018). Taken together, I believe more research needs to be completed to uncover the role of tDCS in improving movement through contributing to more accurate state predictions before during and after movement execution.

Transcranial alternating current stimulation relies on a similar neural framework to tDCS. But, in contrast to tDCS, tACS endeavors to capitalize on the cortical oscillations that are seen in different neural systems (the same brain waves measured with EEG). The basic goal of tACS is to interfere with these rhythms and modulate cortical excitability in a frequency-specific manner (Dissanayaka, Zoghi, Farrell, Egan, & Jaberzadeh, 2017). Miyaguchi and colleagues have published many promising findings using tACS to deliver an alternating current between the primary motor cortex (M1) and the cerebellum while participants learn different motor skills (Miyaguchi et al., 2020; Miyaguchi et al., 2018; Miyaguchi et al., 2019). As we've described, the cerebellum is highly involved with sensory input and sensory predictions while M1 is largely responsible for issuing conscious motor signals to the lower motor neurons involved in a task. Miyaguchi and colleagues have consistently shown that this alternating current benefits motor performance and motor learning of various motor skills. The cerebellum and M1 communicate through cortical projections to the cerebellum to calculate the most likely state of the effector limb based on the outgoing motor command. The discrepancy between expected sensory consequence and actual feedback is then communicated back to the M1 to assist in subsequent motor actions (Miall & Wolpert, 1996; Shadmehr & Krakauer, 2008; Wolpert et al., 2011). These findings suggest that tACS could help to strengthen this neural circuit to calculate more accurate sensory predictions. Additionally, the PMBS has shown to index confidence in internal models (Tan et al., 2016; Tan, Zavala, et al., 2014). I believe future work should endeavor to exploit the role of the PMBS in motor learning to promote correct movements via tACS assisting the CNS is constructing accurate forward models.

The exact neural mechanisms effected by tDCS and tACS alone have yet to be clarified and additional research is needed to identify standard protocols of use. Initial findings with these technologies indicate that there is potential to impact motor performance. Whether they can be reliably implemented to improve skilled motor performance will be seen as more research is done in coming years. Of note, it should be mentioned that tDCS and tACS promote neural plasticity to strengthen consistently executed neural patterns. However, this works under an unsupervised learning mechanism that is not governed by a distal teacher communicating error signals. Thus, in the framework that tDCS/tACS does in fact work to improve motor learning, if incorrect movements are consistently occurring while receiving this stimulation, incorrect neural pathways will be promoted to hinder the correct movement. Accordingly, it is important to ensure correct movements are being learned while utilizing tDCS/tACS.

An alternative use of electric stimulation applies electrical stimulation to sensory nerves in the periphery. Transcutaneous electric nerve stimulation (TENS) can be used to excite heavy myelinated sensory fibers in the peripheral nervous system. This serves to prime the ascending sensory pathways that relay somatosensory information to the brain. Almuklass et al. applied TENS to patients with multiple sclerosis and reported an immediate improvement in motor performance of gait and balance as well as fine motor skills (Almuklass, Capobianco, Feeney, Alvarez, & Enoka, 2019). Additionally, Elboim-Gabyzon et al. (2019) showed that patients recovering from hip surgery walked further during a 2-minute walk test when receiving TENS than a group that received no stimulation. In a review article including 11 studies that applied TENS to stroke survivors to improve mobility, Kwong et al. (2018) concluded that TENS is beneficial towards mobility and walking in stroke patients as well as improves their walking capacity.

In reference to an earlier section, TENS may serve to increase the quantity and quality of sensory information coming from somatosensors in the periphery and to decrease the delay between sensory stimulation and central processing. This improvement in the incoming sensory data gives the CNS a better opportunity to calculate the correct location of their body parts as they perform various motor skills. I believe that TENS is a promising method of improving sensory function that is cost-effective and easy to apply in clinical or healthy populations. I also believe that because such elaborate neural processes are put in place to extract relevant data from the inherently noisy sensory data, the least bit of improvement at the lowest level may provide the means for large improvements in movement capabilities.

Virtual reality

Virtual reality (VR) and augmented reality (AR) have received substantial attention in recent years due to the increased availability of inexpensive AR/VR headsets and user-friendly software platforms that allow custom AR/VR protocols. Simply put, VR involves an artificial environment containing visual information that allows natural behaviors to emerge (Felsberg, Maher, & Rhea, 2019). AR systems merge computer-generated virtual objects with real world scenes (Wang & Wang, 2017). These technologies allow the researcher/practitioner to provide ecologically valid scenarios in a safe environment that can be shaped to the needs and skill level of each individual (de Bruin, Schoene, Pichierri, & Smith, 2010). Generally, somatosensation, vision and the vestibular system are predominantly relied upon to control motor skills. AR and VR are particularly beneficial towards assessing/improving somatosensation because AR and VR technologies give practitioners complete control over visual feedback permitting researchers to remove visual feedback of body position and force a reliance on somatosensory and vestibular sources. In the past, proprioception has been trained/assessed while individuals' eyes are closed, forcing a complete reliance on proprioception (Han et al., 2016b). However, most movements that involve proprioception also require interaction with objects within the environment. VR is an optimal tool for improving proprioceptive function because it allows complete control over visual input throughout the performance of a motor task. As a result, training protocols can be created with specific movement goals requiring interaction with objects in the environment. And, while maintaining visual feedback on the object's location(s), visual feedback of their own body can be systematically manipulated, forcing the CNS to rely on proprioceptive sources when planning, coordinating and executing the movement.

In clinical populations, VR has been effectively used as a rehabilitation tool to improve motor function, predominantly with stroke (Felsberg et al., 2019). Cho et al. and Kim and colleagues have demonstrated that VR can be effective towards improving proprioception in stroke patients by practicing upper extremity tasks with controlled visual feedback of their arms as they trained (Cho et al., 2014; Kim et al., 2013). Similar findings have also been shown in full body gait protocols (Lewek, Feasel, Wentz, Brooks, & Whitton, 2012; Virk, McConville, & Ieee, 2006). By limiting visual feedback of one's own body throughout the performance of a goal-directed movement, the estimation of body state is heavily based on proprioceptive sensory information and predictions. As a result, the CNS must adapt to become more effective at using proprioceptive information when controlling movements. Similarly, Cyma-Wejchenig et al. (Cyma-Wejchenig, Tarnas, Marciniak, & Stemplewski, 2020) developed a VR training protocol to specifically trigger proprioception in construction workers whose jobs require them to work at high altitudes where impaired balance abilities may lead to injurious or fatal accidents. The authors showed that six weeks of proprioceptive training in VR significantly improved their static balance on a force plate placed at ground level as well as static balance on a force plate placed at an elevated position.

I believe VR is an optimal tool to improve sensory controlled movements. Of note, with the ability to control the reliance on proprioceptive movement control, a combination of VR with one (or more) of the above-mentioned stimulation techniques could promote neuroplastic adaptations towards identifying the correct sensory information that accompanies optimal movement. I believe that further advancements in technology will continue to provide additional methods that VR can be used to train the proprioceptive system as well as assess it in clinical and healthy populations.

Conclusion

Skilled motor performance can't exist without sufficient somatosensory input. In this introduction, I have articulated many perspectives to stress the immense benefits that somatosensation provides to motor control. Due to these various perspectives that I've mentioned, I believe there is much potential to improve motor performance by specifically targeting sensory function with rehabilitative practices and therapeutic technologies/devices. However, to be able to properly measure the effect of these therapeutic and rehabilitative practices, accurate and robust methods for measuring their impact on motor performance need to be developed. The following chapters will describe three successive studies that I have completed to address these knowledge gaps in the current literature.

My first study will assess whether the Bayesian model of body position estimation is a valid method of psychophysical assessment to assess body position awareness in a full body ecologically valid motor task. Bayesian inference in motor control has been well established in simple upper extremity movements. When assessing behavior to infer body state perceptions that result from sensory information, controlled task familiarization, many trials, and constant variability are needed to form an accurate estimate for a person's sensory function. The current methods that have been used to assess Bayesian inference in motor control account for all three of the necessities though they have not been utilized in a way to assess sensory function in common daily movements. This first study will determine if the Bayesian model of motor control is consistent in a full-body stepping movement.

The second study included in this dissertation will clarify whether ideal Bayesian position estimates are seen in individuals with superior sensorimotor control. Much research has been done to understand the scope of how this statistical model of probability applies to body position estimates in motor control. However, there has been very little work to translate this research towards improving motor performance in various populations. By assessing the Bayesian framework in individuals with superior sensorimotor control, we can establish a standard to compare additional populations in assessing how they behave in this assessment.

The final study of this dissertation will assess the impact of a therapeutic technology on the Bayesian framework and ultimately their ability to use somatosensory information as they perform the Bayesian assessment. I mentioned previously that there is a need for more specific methods of assessing sensory functions to measure the impact of therapeutic approaches aimed at improving sensory function. This study will measure the impact of transcutaneous electric nerve stimulation (TENS) applied on the muscles of the legs to minimize somatosensory uncertainty of a full body stepping movement.

This collection of studies will demonstrate a novel method and approach towards assessing sensorimotor function and the use of sensory information in skilled motor performance. Using psychophysical methods of assessing behavior in a stepping movement, I provide a quantitative way at measuring the amount that individuals rely on their sensory information during this movement as well as their own perceived uncertainty in the movement decisions they make. I explain how uncertainty in sensory information impacts the degree that individuals rely on learned expectations for the state of their bodies and how their movement decisions are impacted by sensorimotor expertise and electric stimulation. I intend the results of these studies to inform future methods of measuring sensory uncertainty in all populations, enlighten our understanding of the neural processes involved with elite motor performance, and provide explanation for any observed benefits or hindrances that come with therapeutic interventions aimed at impacting somatosensory function.

CHAPTER 2 – BAYESIAN INFERENCE IN A FULL-BODY STEPPING MOVEMENT TO ESTIMATE CENTER OF MASS POSITION

Introduction

One's capacity to move within their environment and perform daily tasks is strongly related to actual and perceived quality of life across many healthy and clinical populations (de Paula, Sawada, Nicolussi, Andrade, & Andrade, 2013; Forhan & Gill, 2013; Musselwhite & Haddad, 2010). An important contributing factor to a person's mobility is their aptitude to maintain upright balance. Balance is accomplished by keeping the vertical projection of the center of mass (CoM) within the boundaries of the base of support (often defined by the outer boundaries of the feet). Impaired balance leads to reduced quality of life across many populations (Haider et al., 2016; Maki, Holliday, & Topper, 1994) due to the increased risk of falls that accompanies impaired balance (Cattagni, Scaglioni, Laroche, Gremeaux, & Martin, 2016; Fernie, Gryfe, Holliday, & Llewellyn, 1982; Maki et al., 1994; Mignardot, Beauchet, Annweiler, Cornu, & Deschamps, 2014). Indeed, postural sway is larger in older adults with a recent history of falls (Fernie et al., 1982; Mignardot et al., 2014; Simoneau, Billot, Martin, Perennou, & Van Hoecke, 2008). Furthermore, falls are the leading cause of fatal and non-fatal injuries among adults sixty-five years of age and older ((WISQARS), 2018). In contrast, superior balance ability leads to enhanced athletic performance and fewer lower limb injuries (Han, Anson, Waddington, Adams, & Liu, 2015; Hrysomallis, 2007, 2011; Kiers, van Dieen, Dekkers, Wittink, & Vanhees, 2013). As follows, a person who is better at controlling the movement of their CoM will be more effective in their overall motor performance than those with inferior balance control.

Because balance is accomplished by maintaining the CoM within the boundaries of the base of support, an accurate and up-to-date estimate for the CoM's location is essential to ensure effective mobility and avoid harmful falls. This estimate is informed by sensory information received by the central nervous system (CNS) from various sources with a heavy emphasis from vision, proprioception, and the vestibular system. The CNS takes in information from all these sources and combines them to form the best estimate for the location of the CoM as we perform daily mobility related tasks. Visual input informing body position may simultaneously be informing the CNS of visual cues in the environment specific to the current task such as where to turn, or who is approaching that we'd like to interact with. Similarly, somatosensory inputs that inform proprioception and body position awareness may also be used to provide input for objects we interact with such as a phone or dog leash. Thus, it is the task of the CNS to put emphasis on the sensory sources that are most important to the balance task at hand. Sensory re-weighting theory suggests that the CNS shifts reliance to more reliable sources of sensory input to optimize balance control (Han, Anson, et al., 2015; Pasma, Boonstra, Campfens, Schouten, & Van der Kooij, 2012). Nevertheless, even in the most ideal scenarios, there remains a degree of uncertainty in all sensory information received by the CNS to control balance.

All afferent information received by the CNS is accompanied by unavoidable uncertainty (Faisal et al., 2008). For example, proprioceptive sensory data is merely the result of firing peripheral receptors and not a direct measurement of the parameter of interest (e.g. joint angles, limb position, velocity etc.) (Bays & Wolpert, 2007). Also, the numerous degrees of freedom of the human body combined with inherent dynamics in the environment ensure that no motor plan is ever duplicated in exactness. Consequently, each movement is accompanied by a unique dataset of resultant sensory information. As follows, the estimation of the current state of the body cannot be as simple as 'a + b = c'. Rather, the CNS must infer the most likely body state from uncertain sensory evidence and use it to choose a motor plan that is most likely to assist in meeting the task demands. This process is further complicated when you consider the impairments to sensory function that occur in healthy aging or because of disease or injury (Cameron et al., 2008; van Hedel & Dietz, 2004; Vidoni & Boyd, 2009; York et al., 2009). Overall, the ambiguity and uncertainty that is inherent to sensory information prompts many questions as to how the CNS effectively coordinates smooth and precise movements (Yuille & Kersten, 2006). That healthy individuals can balance and walk with little difficulty signifies that the CNS has become proficient at decoding this sensory puzzle, yet the exact mechanisms remain to be seen.

In 2004, Kording and Wolpert suggested that the CNS may address sensory uncertainty in a way that is consistent with a statistical model known as Bayesian inference when coordinating movement (Kording & Wolpert, 2004a). Bayesian inference posits that when estimating a certain parameter (e.g. CoM position), the most probable value comes when we combine the current dataset (incoming sensory data) with previously recorded data (learned expectations of CoM position) (Bayes, 1763; Freedman, 1996). In the context of sensory-driven motor control, the CNS estimates the most probable state of a body part given the current sensory information from vision and proprioceptors as well as learned expectations of body position based on many previous movements. In this framework, when controlling a movement, if the current sensory information is more variable/less certain, more weight will be placed on learned expectations when forming a decision on where a body part is (figure 1.2). Conversely, if sensory information conflicts with learned expectations, but is more certain, more weight will be placed on the current sensory information when forming a decision for where a body part is.

While initial findings on this topic are promising, they predominantly involve one-dimensional upper-body tasks (Chambers, Sokhey, Gaebler-Spira, & Kording, 2018; Darlington, Beck, & Lisberger, 2018; Jarbo, Flemming, & Verstynen, 2018; Palmer, Auksztulewicz, Ondobaka, & Kilner, 2019). Typical human behavior requires movements in many directions involving multiple joints and body parts. Specifically, gait and balance are both imperative to quality of life and functional independence. As follows, it is important to clarify how the CNS addresses uncertainty when controlling balance. The purpose of this project was to determine if the CNS controls full body, multi-directional stepping tasks in a way that is consistent with the Bayesian framework that has been shown in simple upper extremity movements. I hypothesized that as sensory information becomes uncertain, the CNS relies more on learned expectation for CoM position when forming a decision for its current state. In addition, I expected that the uncertainty of participants' responses would also increase as the sensory information they received became less certain. The results from this study will inform our understanding of how CoM position is estimated by the CNS as well as provide a vital model that can be used to measure sensory uncertainty across many populations.

Methods

Participants

A total of 57 young adult females participated in this study (age range, 18-31 years; mean age 21.9 ± 2.3 years). All participants were healthy with no serious injuries or ailments limiting their physical abilities. A complete description of participant demographics and characteristics can be found in Table 2.1.

Table 2.1 Demographics and Participant Characteristics

variable	Min.	Max.	Mean	St. Dev.
Age (years)	18.0	31.0	21.9	2.3
BMI	19.5	30.7	23.5	2.6
Exercise (min/week)	25.0	1,200.0	392.9	266.5
Height (inches)	61.0	74.0	66.7	2.9
Weight (lbs.)	110.0	220.0	148.8	20.0

BMI = Body mass index reported in kilograms of body mass per squared meter

Study Protocol

Participants came into the lab for a single two-hour visit where they completed a virtual reality motor learning protocol based off the methods from (Kording & Wolpert, 2004a) but adapted to a full body stepping motion. This study was approved by the Colorado State University Institutional Review Board, and all participants provided written informed consent prior to participation.

Virtual Reality Motor Learning Protocol

Setup

Upon arrival at the lab and following the informed consent process, each participant was prepared for participation in the virtual reality protocol (Figure 2.1). This process began by placing two reflective markers on distinct locations on their body for motion capture purposes (Figure 2.1 A). The first marker was placed at the location of each participant's center of mass. Previous research has shown the CoM location to equal fifty six percent of the body height for young adult active females (measured from the ground) (Virmavirta & Isolehto, 2014). Accordingly, the first marker was placed at that specific location based on their own height. The second marker was placed on their greater trochanter to determine the step length that would be used in the protocol. For each trial within the protocol, participants stood in a balanced stance in the middle of the assessment area while wearing the virtual reality headset (Oculus Rift S, Facebook Technologies LLC, Irvine CA). Vicon motion capture cameras continuously collected the 3-dimensional positions of the two reflective markers placed on their CoM and left greater trochanter and live streamed with Vicon Tracker software (Vicon Motion System Ltd., Yarnton, England, UK) into the VR environment (Unity Software Inc., San Francisco, CA). All behavior within the Unity virtual environment was created with custom scripts written in C# language.

Training Block

The purpose of this protocol was to assess the degree that participants rely on their expectations of CoM position when sensory information is uncertain during a full body stepping motion, as well as measure the effect that sensory uncertainty has on overall position uncertainty as participants estimate their position. Thus, I needed to

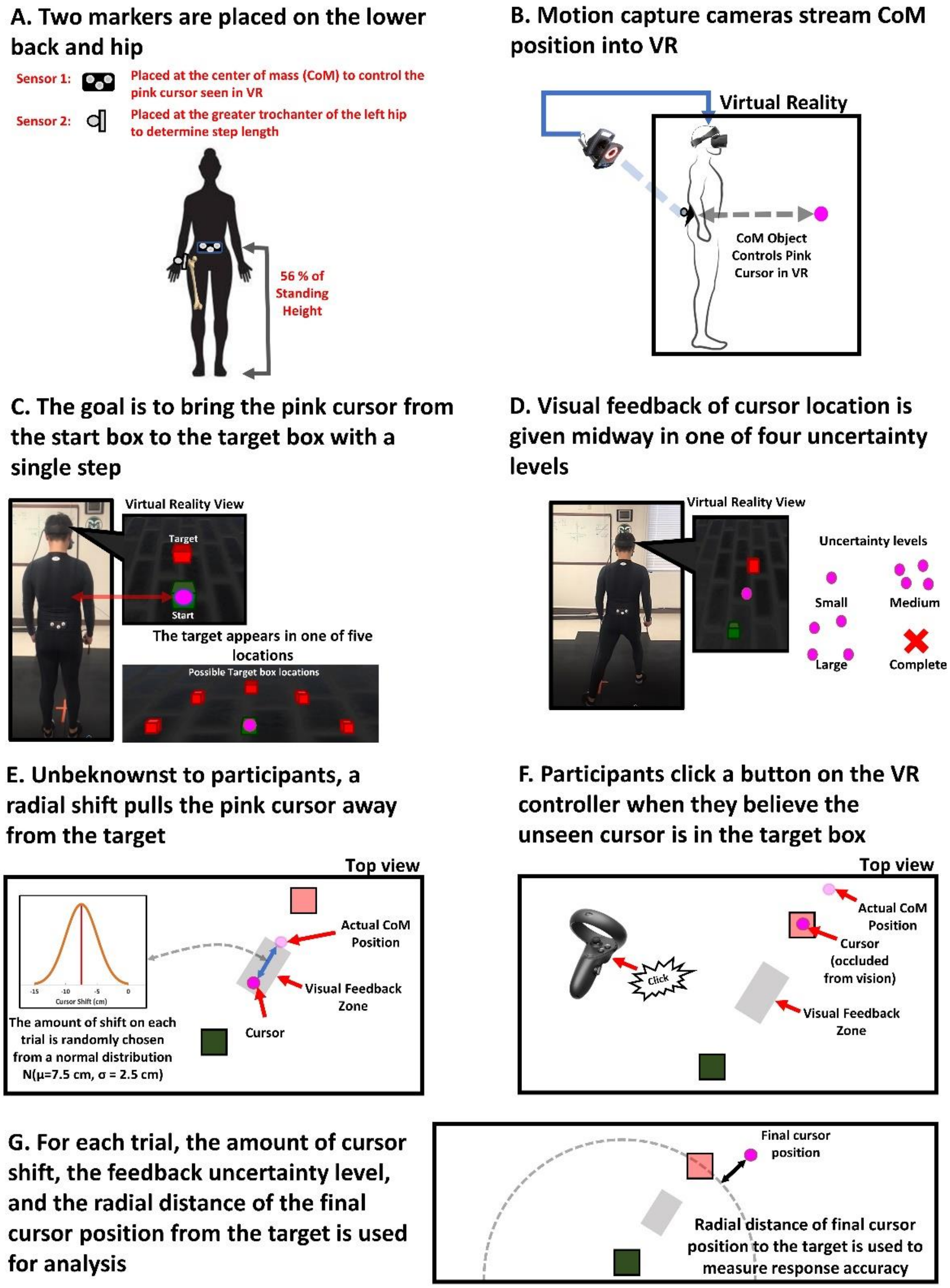


Figure 2.1. Virtual reality protocol details.

control for the fact that each participant enters the lab with their own unique positional expectations. As follows, I first needed to get participants on the same page and have similar expectations for the whereabouts of their CoM as they perform the steps included in this protocol. To achieve this expectation, I first had participants complete a training block where they were able to learn certain characteristics of the motor task prior to the assessment blocks.

For each trial within the training block, participants stood in a balanced stance in the middle of the assessment area. In virtual reality, participants see a pink sphere directly in front of them (Figure 2.1 B). The behavior of that pink sphere is controlled, in real-time, with the reflective marker worn on their CoM. The pink sphere (which will be referred to as the cursor) begins within a green start box at the beginning of each trial (Figure 2.1 C). A red target box appears in one of five locations (0°, 45°, 90°, 135°, and 180° from the green start box). The distance in between the start and target boxes was thirty five percent of the vertical distance from the ground to the greater trochanter marker. In this way, the step length to be performed was individualized to each participant. The amount of thirty five percent was chosen during pilot testing for this study and concluded to be a comfortable step length for all participants that mimics a common step length that would be normal in daily life. Participants were instructed to bring the cursor from the green start box to the red target box with a single step with one leg (Figure 2.1 D). The direction and leg used to step changed on each trial since the target angle varied randomly from trial to trial. Participants were also instructed that although visual feedback of the cursor position would only be available partway through the movement, it was consistently there albeit invisible at times. As follows, the instant the cursor left the green start box it was occluded from vision and only made visible partway through the movement (Figure 2.1 D). When participants believe the cursor is in the target box, they push a button with the VR controller and the actual cursor position is revealed to them briefly (Figure 2.1 F).

As previously mentioned, the purpose of the training block was to get all participants on the same page of CoM location expectations. To accomplish this purpose and unbeknownst to participants, a backwards shift was added to the cursor location on each trial as it exited the starting block and was occluded from vision (Figure 2.1 E). As a result, the participant had to move their CoM past the target an amount equal to the backwards shift to place the cursor in the target box. The visual feedback given partway informed participants of the degree of the shift and the amount needed to compensate to hit the target. The shift amount varied on every trial and was randomly chosen from a normal distribution N(μ=-7.5 cm, σ= 2.5 cm). The training block involved five trials performed while receiving verbal instruction from study coordinators and then one hundred trials on their own with the purpose of implicitly learning to compensate for the shift in their movements.

Assessment Blocks

Following the training block, participants completed five more blocks of 100 trials each. The trials within these blocks were very similar to the trials of the training block with the exception of the visual feedback of the cursor position. In the assessment blocks, the visual certainty of the cursor location shown partway through the movement was systematically manipulated. For the majority of trials, the uncertainty level was the same as the training block where they were shown the precise cursor location (referred to as the small uncertainty level). However, on some trials, uncertainty was added to the cursor location by adding 2-dimensional gaussian noise to its location. This noise gave the perception of an approximate area of where the cursor was located. The size of noise varied between two levels (referred to as medium and large uncertainty): N(μ= 0 cm, σ=

2.5 cm) and N(μ= 0 cm, σ= 5 cm). There was also a condition of complete uncertainty where no visual feedback was given at all for the cursor location after it left the start box until the next trial began. On trials where the uncertainty level was either medium, large or complete, no final feedback was given to participants informing them of their accuracy after they pressed the VR controller. This was done to eliminate participants from using final feedback to inform their performance on uncertain trials but rather to be limited to just the feedback received during the movement. The uncertainty level on each trial was chosen randomly, with the relative frequencies of the uncertainty levels (small, medium, large and complete) being (4,1,1,1) respectively for assessment blocks 1 and 2 and (3,1,1,1) for blocks 3-5. The bias of the small uncertainty condition was chosen to ensure participants continued to expect the added shift in their movements.

Analysis

Data Analysis

For the analysis of each participants' data, all the responses from the assessment blocks are plotted with each trial's cursor shift on the x axis and the deviation of the cursor from the target when they pressed the VR controller on the y axis (Figure 2.2 A). Each trial is then sorted by the level of visual feedback uncertainty given partway through the movement (Figure 2.2 B). The first hypothesis is that participants will increase their reliance on their expected CoM location as the sensory feedback that they receive becomes less certain. As follows, this would be shown by the cursor shift influencing participants' responses more as the feedback uncertainty increased. Accordingly, I fit a regression line of the deviation of participants' final cursor position on each trial versus the amount of cursor shift for that trial in each of the four feedback uncertainty levels

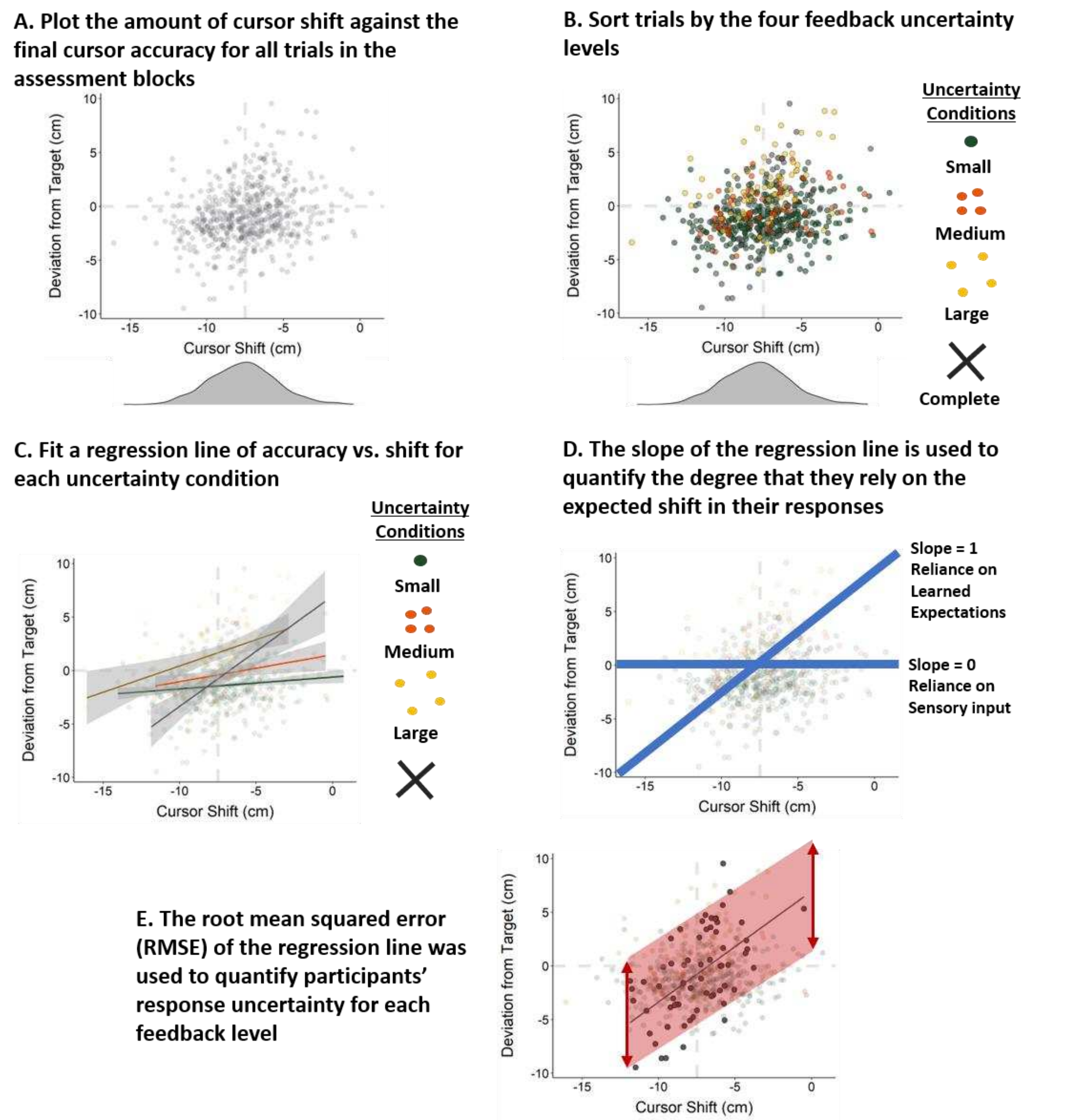


Figure 2.2. Data analysis of virtual reality assessment data.

(Figure 2.2 C). The slope of each regression line is used as a metric to gauge how much each participant is relying on the expected shift in each feedback condition (Figure 2.2 D). A regression line with a slope of zero signifies that the cursor shift had no impact on their final responses and didn't influence their accuracy at all. A regression line with a slope of one would indicate a complete reliance on the shift or, in other words, no matter what feedback they received, they compensated by moving their CoM 7.5 cms past the target. I expected that reliance on the shift would increase as feedback uncertainty increased which would be displayed as a gradual increase from 0-1 across the four feedback conditions.

Furthermore, I expected that the degree of uncertainty in the feedback given during a trial would lead to uncertainty in participants' responses and that it would increase as the feedback uncertainty increased. To quantify uncertainty, I use the root mean squared error (RMSE) of the accuracy vs. shift linear model which displays the spread of the data along the regression line (Figure 2.2 E). Obviously, there are many things that lead to variability along a regression line. However, the only variable that changes across these test conditions is the certainty of the visual feedback given to inform participants of their CoM position. As a result, the change in RMSE across conditions can only be due to participants becoming more uncertain/less certain of their responses. This method of measuring uncertainty has been reliably shown in previous research (Kording & Wolpert, 2004a, 2004b).

Statistical Analysis

All statistical analysis was conducted in R software (version 4.1.1) with an alpha level set at 0.05. To ensure statistical assumptions were met prior to running any statistical tests, assessments of normality and equality of variance were performed on all outcome metrics of this study such as: Shapiro-Wilk tests, QQ plots and plots of the residual vs. fitted data. These assessments indicated that measurements of slope and uncertainty all met the assumptions needed and were included in the analysis.

To assess differences in the slope of the regression line for all 57 participants across the four feedback uncertainty levels, a one by four repeated measures analysis of variance (ANOVA) was performed with random effects to account for each participant being represented by more than one observation within the analyzed data. The independent variable for the ANOVA was the four feedback uncertainty levels (small, medium, large and complete). To identify specific differences between conditions, follow up pairwise comparisons were calculated using Tukey's honest significance test. The same statistical model was used for the second hypothesis but with the uncertainty measurement (RMSE) as the response variable.

Results

In total 57 neurotypical healthy female participants were included in the final analysis. Characteristics of all study participants are presented in table 2.1.

Learning to Compensate for The Cursor Shift

On each trial performed in the study protocol, a backwards shift was added to the cursor location forcing participants to move their CoM past the target an amount equal to the shift for them to bring the cursor into the target box. Also, the degree of shift varied on each trial and was randomly chosen from a normal distribution N(μ= -7.5 cm, σ= 2.5 cm). Accordingly, the ideal distribution of the participants' final CoM position would mirror the distribution of the shift (N(μ= +7.5 cm, σ= 2.5 cm)). The ideal distribution would imply that participants perfectly learned to expect the shift and compensated for it successfully in their trials. As can be seen in Figure 2.3, the final CoM position for all trials from all participants is very similar to the ideal distribution. In fact, to demonstrate that participants

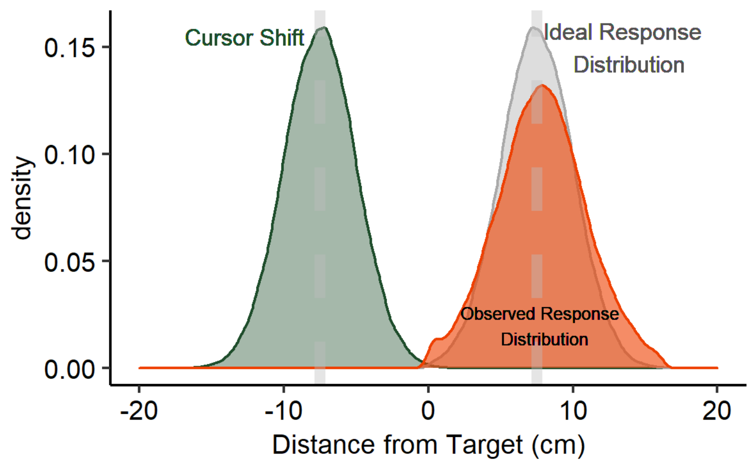


Figure 2.3. Density distributions of the cursor shift (green) and final CoM location (orange) for all trials from all participants. The ideal distribution is also shown (gray) to demonstrate how well participants learned to compensate for the cursor shift.

had learned to compensate for the shift in their movements, I conducted a one-sample t test for the average CoM position for all participants after completion of the study. Results from the one sample t test indicated that there was not enough evidence to conclude that the expected cursor shift was not equal to 7.5 cm ($t(56)= -0.829$, $p = 0.4107$). This result suggests that participants did indeed expect a 7.5 cm backwards shift to the cursor when moving to the target.

Reliance on Expected Shift and Uncertainty

As can be seen in figure 2.4 showing the data from one individual participant, the slopes of the fitted regression lines increase as the feedback incertainty increases. This implies a greater reliance on the expected cursor shift when estimating their CoM position and a gradual disregard for the visual feedback given as that feedback becomes more uncertain. Similarly, when I combined the data from all participants in the repeated

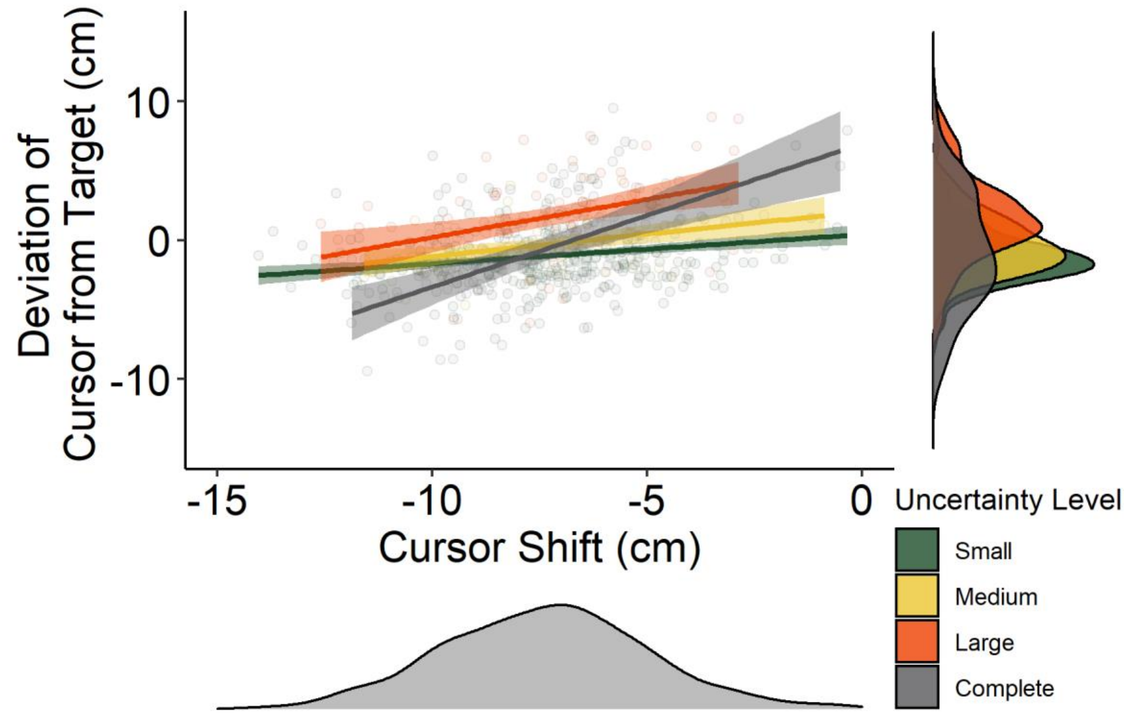


Figure 2.4. Cursor accuracy and cursor shift on every trial for one representative participant. Fitted regression lines indicate an increase in slope as feedback uncertainty increases. The density plots to the right also indicate greater variability in this participant's responses as feedback uncertainty increases.

measures ANOVA, I found a significant main effect of feedback uncertainty level on participants' reliance on the expected cursor shift ($F(3,168) = 118.84$, $p < 0.001$). Follow up pairwise comparisons with Tukey's honest significance test (Figure 2.5 A) indicated significant differences of reliance between the small and medium feedback uncertainty levels ($p < 0.001$), the small and large feedback uncertainty levels ($p<0.001$), the small and complete feedback uncertainty levels ($p < 0.001$), the medium and complete feedback uncertainty levels ($p < 0.001$), and the large and complete feedback uncertainty levels ($p < 0.001$). Their was not enough evidence to conclude a significant difference of reliance in the medium and large feedback uncertainty levels with alpha = 0.05 ($p = 0.0657$). Taken together, these results confirm the first hypothesis that learned expectations for CoM position would influence CoM position estimates during a full body stepping task as uncertainty of the incoming sensory information increased.

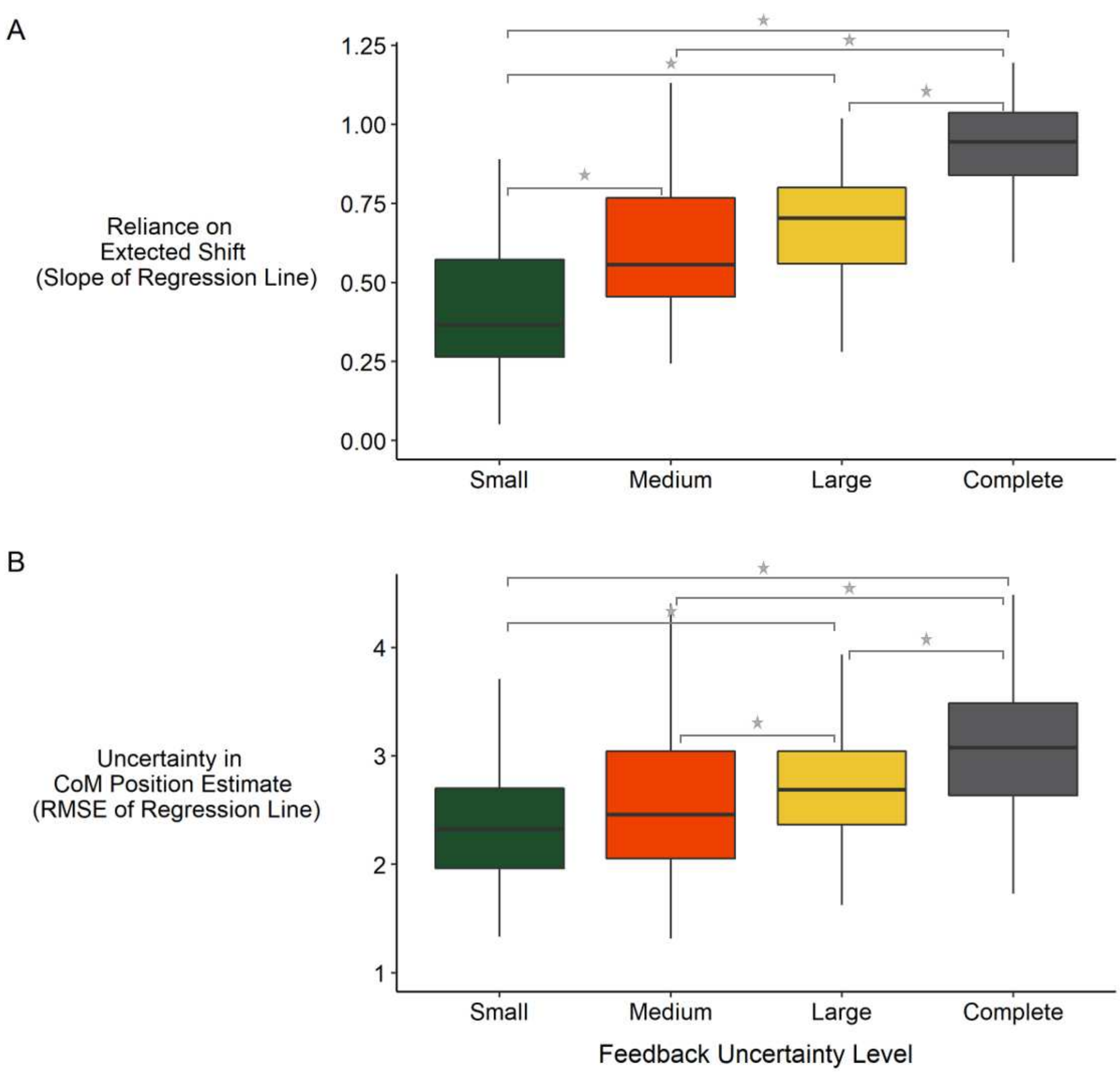


Figure 2.5. Boxplots for the reliance and uncertainty measurements across feedback uncertainty levels. A. Reliance on the expected body position increased as feedback uncertainty increased showing that the degree of uncertainty within the incoming sensory data does influence how much it informs body position estimations. B. Uncertainty in participants' responses increased as the feedback they received became less certain. ★= p <.006.

The second hypothesis of this study was that participants would demonstrate more uncertainty in their assessment responses as the feedback uncertainty increased. I defined response uncertainty as the RMSE of the regression line of the linear fit between response accuracy and the cursor shift on each trial for each feedback uncertainty condition. Similar to the first hypothesis, I performed a one-way repeated measures ANOVA with random effects to identify the effect of feedback uncertainty on participants' response uncertainty. Results from the repeated measures ANOVA identified a significant main effect of feedback uncertainty level on response uncertainty ($F(3,168) = 41.981$, $p < 0.001$). Follow up pairwise comparisons with Tukey's honest significance test (Figure 2.5 A) indicated significant differences of uncertainty between the small and large uncertainty levels ($p < 0.001$), the medium and large feedback uncertainty levels ($p = 0.005$), the small and complete feedback uncertainty levels ($p < 0.001$), the medium and complete feedback uncertainty levels ($p < 0.001$), and the large and complete feedback uncertainty levels ($p < 0.001$). Their was not enough evidence to conclude a significant difference of reliance in the small and medium feedback uncertainty levels with alpha = 0.05 ($p = 0.1671$). Taken together, these results confirm the second hypothesis that uncertainty in sensory feedback would lead to more uncertainty in CoM estimates as participants perform full-body stepping movements.

Discussion

The purpose of this work was to determine if the CNS controls full body multi directional stepping tasks in a way that is consistent with the Bayesian framework that has been shown in simple upper extremity movements. These results show that Bayesian inference is indeed a reliable model to apply towards understanding how the

CNS monitors CoM position during a full body stepping movement. As a result, this means that uncertainty accompanying incoming sensory data impacts how much weight is placed on it in the CoM position estimate. Also, these results imply that learned expectations for where the CoM has been during previous movements of a similar type inform the position estimate made by the CNS during stepping tasks.

I expected that the degree to which learned expectations for CoM position influenced the final position estimate would increase as the incoming sensory input became less certain. These results are in line with previous work showing Bayesian inference in simple upper extremity reaching tasks (Hewitson, Sowman, & Kaplan; Kording & Wolpert; Vilares & Kording). Stevenson and colleagues (Stevenson, Fernandes, Vilares, Wei, & Kording, 2009) found that center of pressure (CoP) application during a one-dimensional balance task fit the Bayesian framework accounting for visual uncertainty. These results add to the current work by showing the CoM position is also estimated in a way that fits the Bayesian framework. In addition, the motor task involved in this study involved three-dimensions of movement stepping to multiple targets at different angles. This involved building expectations for CoM behavior in one direction and applying it to different targets with the same radial distance. Work done by both Hewitson et al. (2018) and Fernandes et al. (2014) has found that position expectations built in one movement can generalize to similar movements either with an opposite limb or a nearby target. This work confirms that this behavior is also consistent in the lower body. Whether learned expectations built in upper extremity movements can generalize to movements of the lower body will be the focus of future research. If this is the case, it may be an effective method of rehabilitation for injuries or impairments that limit the functionality of a limb.

Furthermore, I anticipated that participants would show more uncertainty in their CoM estimates when their available sensory information became uncertain. Using the RMSE of the relationship between the cursor shift and the cursor accuracy, I showed that participants did in fact show more uncertainty when estimating their CoM position. Uncertainty in incoming sensory data is impossible to eliminate. Light conditions, disease, injury and many other conditions lead to uncertainty in the sensory information our CNS receives. Combining the data that we receive with our learned expectations is a way that the CNS can compensate for this unavoidable uncertainty and still minimize the overall uncertainty in our position estimates. Using this method, we have a quantifiable way of measuring how confident a person is on where their CoM is. This metric could be used to measure the efficacy of rehabilitative practiced aimed specifically at improving sensory function. The majority of methods used to measure sensory function are applied at the peripheral level (Han et al., 2016b). While these methods have shown promise, combining them with this new metric of uncertainty may provide crucial insight into how sensory information is integrated and used by the CNS.

There has been much work done in recent decades on estimating the CoM position from the researchers perspective (Cotton, Murray, & Fraisse, 2009; Cotton et al., 2011; Rabuffetti & Baroni, 1999; Schinkel-Ivy, Komisar, & Duncan, 2020). When considering how balance is accomplished, it makes sense that the scientific community would be interested in knowing exactly where the CoM is as we perform mobility related tasks. As follows, the behavior of the CoM is used to indicate balance ability across many populations (Pasma et al.; B. S. Richmond, Fling, Lee, & Peterson). Furthermore, much work has also shown that motor plans during mobility are created to prioritize a smooth trajectory of the CoM (Bucklin, Wu, Brown, & Gordon; Hicheur, Vieilledent, Richardson, Flash, & Berthoz; Welch & Ting). There has also been much work to explain how sensory information is integrated and processed by the CNS to control balance (Forbes, Chen, & Blouin, 2018; Peterka, 2018). With so much emphasis on the importance of the CoM to control balance, there is a lack of research on how the CNS monitors and estimates CoM position during balance.

I show here that the CNS estimates CoM position in a way consistent with Bayesian inference by accounting for the uncertainty of sensory information and relying on learned expectations from previous balance attempts. Overall, I believe this information will help understand how CoM behavior influences overall body position awareness and ultimately lead to a greater understanding of mobility across all populations.

CHAPTER 3 – IS BAYESIAN INFERENCE IN A FULL-BODY STEPPING MOVEMENT BENEFICIAL TO OVERALL MOTOR PERFORMANCE?

Introduction

Daily life requires movements of many types. Whether it be reaching to grab a bottle of water or avoiding a collision with a fellow shopper at the grocery store, each movement requires us to adapt to unique criterion to ensure the task is carried out properly. When reaching for the water bottle, it's location, other objects in the way, one's body position and fatigue level (among many other factors) are constantly varying and must be accounted for as the central nervous system (CNS) creates a motor plan to perform the movement. In the example at the grocery store, more variables are added due to the introduction of mobility and in-motion regulatory conditions. With the ever-present dynamics that are inherent to goal-directed movement, it is essential that one can adapt to the task demands and create a motor plan that efficiently completes the movement goal. One of the biggest influences on how a motor plan is created is sensory information notifying the CNS of body position at the beginning and throughout the movement. This influence is why Impairments to incoming sensory data often lead to motor errors that frequently bring negative consequences.

Incomplete sensory information leads to uncertainty. In the context of motor performance, this uncertainty involves both the state of our bodies and the external world. There has been much research exploring the deficits in sensory information that result from injury, disease, or aging (Cameron et al., 2008; Carabellese et al., 1993; Cattaneo, Ferrarin, Jonsdottir, Montesano, & Bove, 2012; Kraiwong, Vongsirinavarat, Hiengkaew,

& Wagert, 2019; Lew, Weihing, Myers, Pogoda, & Goodrich, 2010). Accordingly, research has found these populations to have more uncertainty in their movements due to the inadequate sensory data received by the CNS (Arpin et al., 2017; Reyns et al., 2008). Still, uncertainty in motor control is not unique to populations with impaired sensory function. In fact, the human nervous system is challenged with sensory uncertainty to some degree in every movement we make. Differing light conditions, levels of physical and cognitive fatigue, visual and proprioceptive acuity all lead to body position uncertainty in even neurotypical populations (Abd-Elfattah, Abdelazeim, & Elshennawy, 2015; van Beers, Baraduc, & Wolpert, 2002). Furthermore, noise and variability are present in all stages of acquiring and processing sensory information (Faisal et al., 2008). As follows, the CNS must account for the uncertainty in sensory information to minimize uncertainty in the overall body state estimate and effectively complete each motor task.

Bayesian inference is a statistical model that is often used to estimate an unknown parameter when the available evidence is uncertain (Bayes, 1763; Vilares & Kording, 2011). In this model, the current evidence (termed the likelihood) is combined with previously collected data (termed the prior) to create an optimal distribution to estimate the parameter with the least variability (termed the posterior). Kording and Wolpert (2004a) were the first to apply Bayesian inference to motor control to explain how the CNS accounts for uncertainty in sensory data. Since 2004, their work has been expanded into many different areas of goal-directed motor control to better understand the limits to using Bayesian inference to understand sensorimotor control (Darlington et al., 2018; Genewein & Braun, 2012; Kording, Ku, & Wolpert, 2004; Remington, Parks, & Jazayeri, 2018; Roach, McGraw, Whitaker, & Heron, 2017; Sato & Kording, 2014; Shadmehr &

Krakauer, 2008; Stevenson et al., 2009; Vilares & Kording, 2017; Wei & Kording, 2010). Most of this work has sought to understand Bayesian motor control in different contexts of movement. There has been much work done to expand on how the prior is generalized to other types of movement (Chambers, Fernandes, & Kording, 2019; Hewitson et al., 2018; Wolpe, Wolpert, & Rowe, 2014; Yin, Wang, Wei, & Kording, 2019), how it differs when put under a time constraint (Roach et al., 2017; Tassinari, Hudson, & Landy, 2006), and how the Bayesian model differs between types of movement (Kording et al., 2004; Stevenson et al., 2009). Indeed, I showed in chapter 2 that Bayesian inference also can be used to explain how the CNS estimates CoM position during a stepping movement.

While all this work has benefited our understanding of the neural control of movement, there is a lack of research translating what is known about Bayesian motor control to improve movement in any population. Predominantly, most of the current research has sought to understand this model in various movement contexts. Certainly, the search to understand is one of the central goals of science, and even more so for basic research (Frigg & Hartmann, 2020; Rubio et al., 2010). As follows, models and theories are often used in science to better understand the natural world (Cartwright, 1997; Lohse, 2020). However, the pursuit of improving the human experience in one or many populations is also a central goal of science and is the driving purpose of translational science (Zerhouni, 2005). Without testing the Bayesian model across multiple populations and assessing the differences that arise, its predictive power is limited. Is a person at less risk of injury if their movements strongly fit the Bayesian model better than someone who weakly fits the model? Does an individual with movements that are Bayes optimal have a lower probability of being diagnosed with a neurodegenerative disease? A thorough search of the relevant literature yielded only one article using this model to explain motor control in a different population (Vilares & Kording, 2017). This gap in the literature is due, in part, to the fact that it remains unknown whether Bayes optimal movements are associated with better motor performance. Once this knowledge is gained, this well-established theory can be used to assess and improve moto control in all populations.

Individuals who excel at high level sport often can do so because they are able to consistently create and execute motor plans that accomplish the task more effectively than their peers. In sports that involve gross motor skills, this often requires moving the entire body through space and meticulously coordinating the movement of multiple limbs and joints with varying time constraints. These types of movements rely on constant neural communication of afferent sensory information relaying details about speed and position of involved limbs, integration by central and peripheral mechanisms that give meaning and context to sensory cues that can be used to plan future movements, and numerous efferent signals working simultaneously to control the necessary muscle groups. Not surprisingly, high-level athletes have been shown to perform better in almost all these crucial neural processes (Han et al., 2014; Nakata, Yoshie, Miura, & Kudo, 2010; Zwierko, Osinski, Lubinski, Czepita, & Florkiewicz, 2010). In the context of balance and mobility, athletes appear to be less vulnerable to external disturbances and more precise in balance related tasks (Borzucka, Krecisz, Rektor, & Kuczynski, 2020; Snyder & Cinelli, 2020). Similarly, physical activity leads to benefits in the neural control of movement and mobility (Petroman & Rata, 2020; Prakash, Snook, Motl, & Kramer, 2010; Sexton et al., 2016). If making body position estimates in a way that better fits the Bayesian framework is beneficial to motor performance, it would follow that athletic and physically fit individuals would fit the model better than peers that exercise less.

The purpose of this study was to clarify if Bayesian inference in full body stepping movements is beneficial to overall mobility and balance performance. I hypothesized that elite athletes would perform in a way that better fits the Bayesian framework than non-athletic peers and that physically active non-athletes would also fit the model better than their less active peers. Bayesian inference is a statistical model that is used to improve accuracy and decrease uncertainty in the overall estimate. Due to the enhanced neural processes that have been reported in high level athletes, I also expected that the athletic group would demonstrate a smaller amount of uncertainty in their position estimates while performing this full-body mobility task. Also, in line with previous research, I anticipated that the athletic group would demonstrate superior balance performance when compared to the non-athletic group. Finally, I predicted that the degree to which individuals fit the Bayesian framework would be associated with their balance performance regardless of study group.

Methods

Participants

A total of 56 young adult females participated in this study (age range: 18-27 years) and were divided into three groups depending on their athletic participation and physical activity level. The athletic group (ATH) consisted of female athletes who were currently participating in NCAA Division I sports (14 soccer, 4 softball, 2 volleyball, 2 divers). The active group (ACT) were healthy female adults who regularly exercise at a moderate or vigorous intensity more than 150 min/week (exercise amount chosen because of physical activity recommendations from the American College of Sports Medicine (ACSM) (Garber et al., 2011)). The healthy control group (HC) were healthy female adults who were recreationally active but self-reported regularly exercising less than ACSM guidelines. All participants were healthy with no serious injuries or ailments limiting their physical abilities. A complete description of participant and group demographics and characteristics can be found in Table 3.1.

Table 3.1 Demographics and Participant Characteristics

	HC	ACT	ATH	p-value*
n	16	18	22	
Age: Years (mean (SD))	21.6 (1.8)	23.1 (2.1)	20.59 (1.3)	<0.001
Height: Inches (mean (SD))	66.9 (3.4)	65.8 (2.6)	67.17 (2.7)	0.327
Weight: Pounds (mean (SD))	148.9 (16.8)	142.1 (16.3)	153.23 (24.0)	0.220
BMI: Kg/M^2 (mean (SD))	23.5 (2.5)	23.1 (2.5)	23.81 (3.0)	0.683
Exercise: Min/week (mean (SD))	99.6 (42.5)	305.6 (113.7)	679.09 (140.2)	<0.001

HC = Healthy Control, ACT = Active Control, ATH = Athlete

* p values represent the significance level from a group effect in a one-way ANOVA with each respective variable as the response variable

Study Protocol

Participants came into the lab for a single two-hour visit where they completed the virtual reality motor learning protocol previously described in chapter 2 as well as the modified Clinical Test of Sensory Integration for Balance (mCTSIB) (Freeman et al., 2018). This study was approved by the Colorado State University Institutional Review Board, and all participants provided written informed consent prior to participation.

Virtual Reality Motor Learning Protocol

Please refer to chapter 2 for details on the virtual reality motor learning protocol.

Balance Assessment

The modified Clinical Test of Sensory Integration for Balance (mCTSIB) is a clinical test of balance used in many rehabilitation settings to quantify one's ability to maintain standing balance under differing sensory conditions (Freeman et al., 2018; Goble, Brar, Brown, Marks, & Baweja, 2019). It involves four balance trials each lasting 30 seconds where participants are to stand as still as possible for the duration of the trial (Figure 3.1.A). Each trial is designed to challenge the sensorimotor system differently to identify any weaknesses an individual may have in controlling balance. For this assessment, participants stood on a BTrackS portable force plate (Balance Tracking Systems, Inc., San Diego, CA) that continuously collected the position of participants' center of pressure (CoP) throughout each trial. CoP behavior was measured to assess balance control because the CoP reflects the neuromuscular response to maintain stability of the CoM (B. S. Richmond et al., 2021). Participants stood unshod with their feet together and their hands on their hips for the duration of each trial. Trials involve standing directly on the

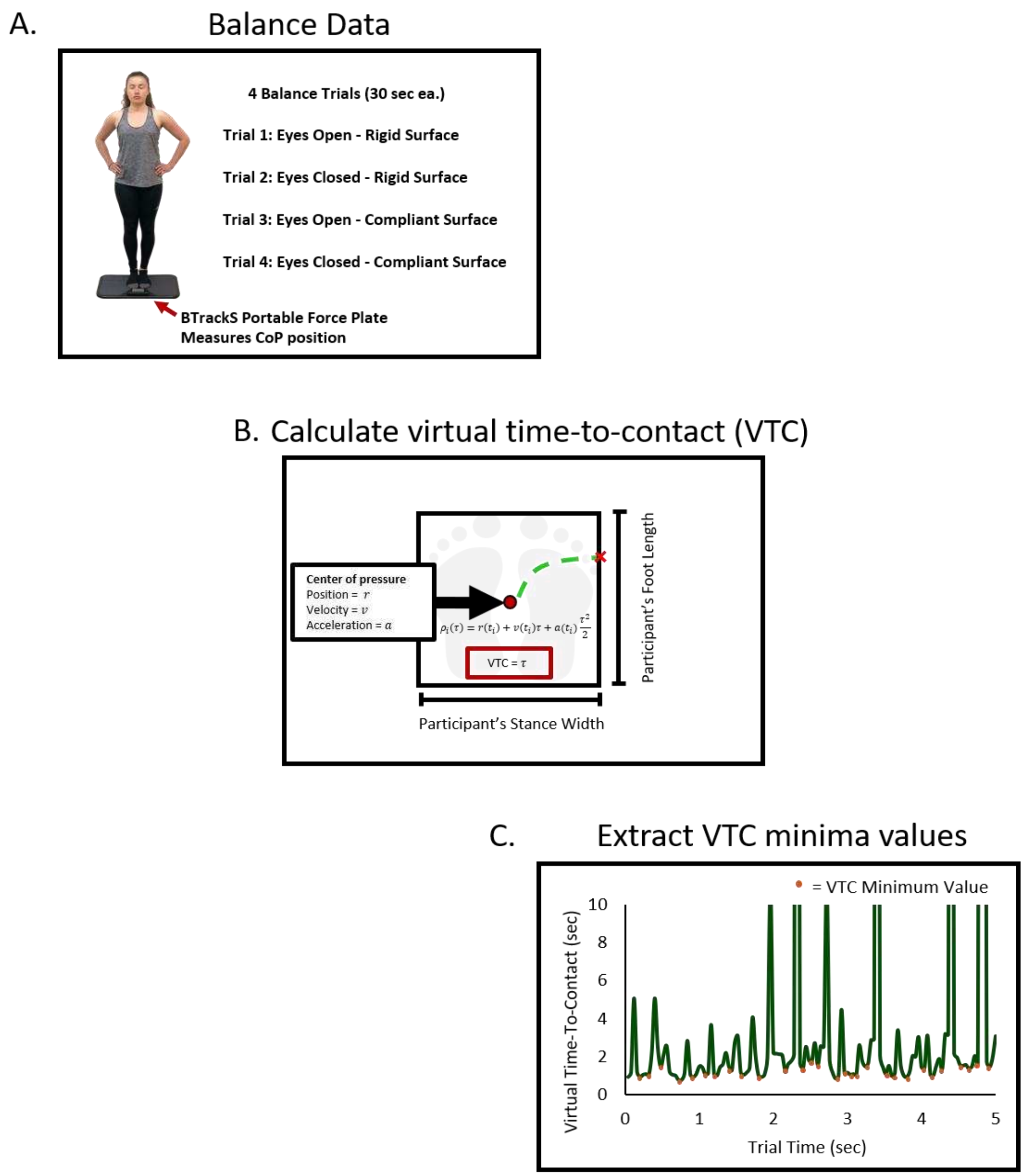


Figure 3.1. Balance collection and analysis protocol. A. Participants complete all trials of the mCTSIB on a BTrackS force plate tracking center of pressure (CoP) behavior. B. VTC is calculated for every time point within a trial. C. Extract the minima values of the VTC signal. The mean of the VTC minima was used in analysis.

rigid force plate with eyes open and closed, as well as standing on a compliant foam pad placed directly on top of the plate with their eyes open and closed.

Analysis

Data Analysis

Please refer to chapter 2 for the analysis used to get the outcome metrics of the VR protocol. Furthermore, to quantify the degree to which each participant fits the Bayesian framework, I developed a measurement I refer to as “Bayes value.” The Bayes value for each participant was calculated by taking the sum of the differences in reliance on the expected shift between the feedback uncertainty conditions (Figure 3.2). Bayesian inference predicts that the body position estimate will progressively rely on the expected shift as feedback uncertainty increases. As follows, I would expect the reliance on the shift to be close to zero in the small uncertainty condition and incrementally increase as feedback uncertainty transitions from small to complete. Ultimately resulting in a complete reliance on the shift in the complete uncertainty condition (reliance equal to 1). In a Bayes optimal individual, this would result in a Bayes value closer to 1 when compared to an individual that does not fit the model as well. The first hypothesis was that the athletic group would perform in a way that better fits the Bayesian model than

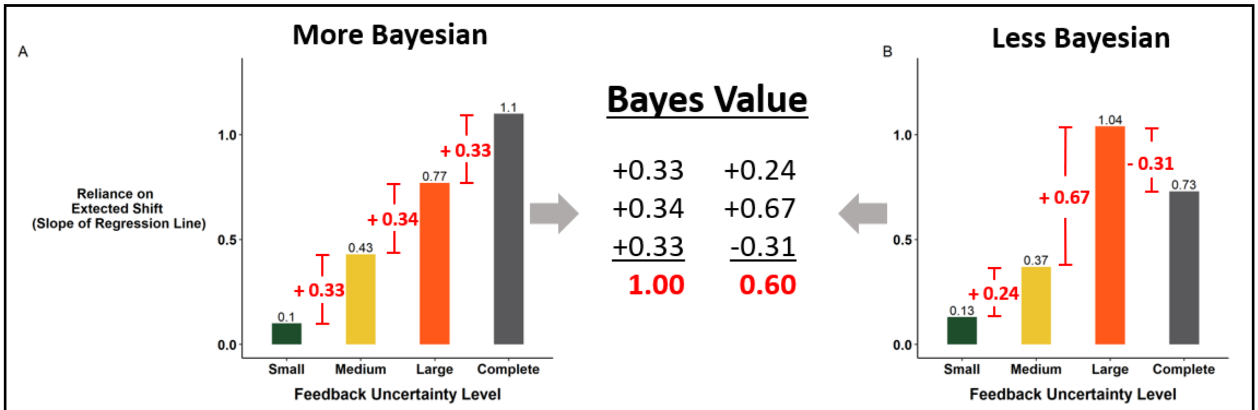


Figure 3.2. Bayes value was calculated by summing the reliance on the expected shift changes that occurred as feedback uncertainty increased. A participant with a Bayes value closer to 1 (A) signifies a greater fit to the Bayesian model than a participant with a smaller Bayes value (B).

non-athletic peers and that the physically active group would fit it better than the less active control group. In this sense, I expected the athletic group to have a Bayes values closer to 1 compared to the other 2 groups and that the active group would report Bayes values higher than the HC group.

With regards to the CoP data from the mCTSIB trials, I calculated the virtual time-to-contact (VTC) for each trial and extracted the minima of the VTC signal to use in the analysis (Figure 3.1). The VTC metric considers the instantaneous position, velocity and acceleration of the CoP, to predict how long it would take the CoP to reach the boundary of the base of support for every data point in a trial. In other words, a lower VTC value means that it would take less time to reach the boundary of the BoS and subsequently fall, thus exemplifying a state of low stability. Previous research has shown VTC to be a superior metric at assessing balance performance in clinical and healthy populations compared to traditional metrics (Hertel, Olmsted-Kramer, & Challis, 2006; S. B. Richmond, Dames, Shad, Sutherlin, & Fling, 2020; van Wegen, van Emmerik, & Riccio, 2002; Whittier, Richmond, Monaghan, & Fling, 2020). The minimum points of the VTC signal represent the points that a motor response is evoked to avoid reaching a point of instability. I used the average of all the VTC minima across a balance trial in the analysis to quantify balance performance.

Statistical Analysis

All statistical analysis was conducted in R software (version 4.1.1) with an alpha level set at 0.05. To ensure statistical assumptions were met prior to running any statistical tests, assessments of normality and equality of variance were performed on all outcome metrics of this study such as: Shapiro-Wilk tests, QQ plots and plots of the residual vs. fitted data. These assessments indicated that all of the outcome metrics used in this study met the assumptions needed and were included in the analysis.

The first hypothesis for this study was that the ATH group would fit the Bayesian framework better than non-athletic groups and that the ACT group would be better than the HC group. This was assessed in two different ways. First, to assess differences in reliance on the expected shift across the feedback conditions, a three (groups) by four (feedback uncertainty levels) repeated measures ANOVA was calculated with random effects to account for each participant being represented by more than one observation within the analyzed data. To identify specific differences between groups, follow up pairwise comparisons were calculated using Tukey's honest significance test. The second way that I assessed the first hypothesis was using the Bayes values from each participant. I conducted a three (group) by one ANOVA to identify differences in Bayes values between the three groups. Similarly, follow up pairwise comparisons were calculated using Tukey's honest significance test to identify specific differences between the three groups.

The second hypothesis was that the athletes would demonstrate a smaller amount of uncertainty in their position estimates while performing the full-body mobility task. To assess this hypothesis, the same repeated measures ANOVA as was used for the first hypothesis but with the uncertainty measurement (RMSE) as the response variable. I used the same statistical model to assess differences in VTC between the three groups across the four balance conditions included in the mCTSIB. I expected that the athletic group would perform better across the balance conditions.

Finally, to assess associations between how well individuals fit the Bayesian framework and their balance performance, I fit a linear model between the Bayes values (response variable) and the VTC minima for the four balance conditions (predictor variables). For any significant associations, the r squared value was used to indicate the strength of the association.

Results

In total, 56 neurotypical healthy female participants were included in the final analysis (22 ATH, 18 ACT, 16 HC). Characteristics of all study participants and groups are presented in table 3.1.

Learning To Compensate For The Cursor Shift

On each trial performed in the study protocol, a backwards shift was added to the cursor location forcing participants to move their CoM past the target an amount equal to the shift for them to bring the cursor into the target box. Also, the degree of shift varied on each trial and was randomly chosen from a normal distribution $N(\mu = -7.5$ cm, $\sigma = 2.5$ cm). Accordingly, the ideal distribution of the participants' final CoM position would mirror the distribution of the shift ($N(\mu = +7.5$ cm, $\sigma = 2.5$ cm)). The ideal distribution would imply that participants perfectly learned to expect the shift and compensated for it successfully in their trials. As can be seen in Figure 3.3, the final CoM position for all trials performed by the ATH group are closer to the ideal distribution, followed by the ACT group and finally the HC group. Taken together, these results suggest that all groups learned the cursor shift with some evidence that the physically active groups learned slightly better than the HC group.

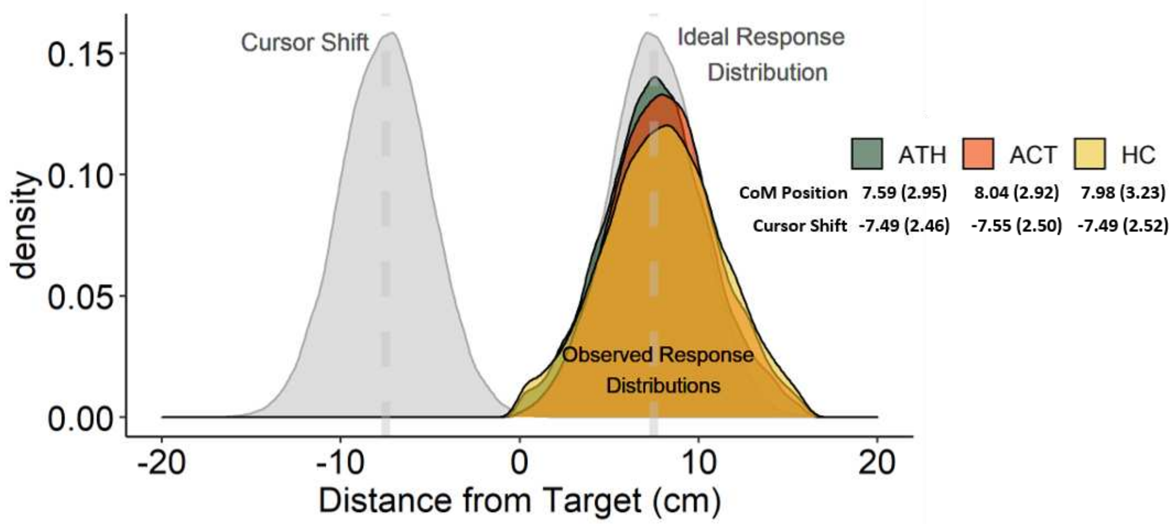


Figure 3.3. Density distributions for all trials within each group. The cursor shift on each trial is randomly chosen from the normal distribution N(μ = -7.5 cm, σ = 2.5 cm). Ideally, participants responses will mirror the shift distribution showing they've learned to compensate for it in their movements. Density plots for each group show the ATH group closest to the ideal distribution, followed by the ACT group and then the HC group.

Reliance On Expected Shift And Bayes Value

Figure 3.4 shows data from two participants and includes only data from the small feedback uncertainty condition. The Bayesian model predicts that the slope of the regression line between cursor shift and response accuracy should be close to zero in this condition, indicating that sufficient sensory data was available to compensate for the cursor shift regardless of its magnitude. From the two participants in Figure 3.4, it is evident that the participant from the ATH group has a slope closer to zero indicating a better fit to the Bayesian model when compared to the participant in the HC group. As can be seen in Figure 3.5.A, this was consistent for both groups as well. I found a significant group by feedback uncertainty level interaction effect ($F(6,159) = 2.80$, $p = 0.013$) indicating that the three groups responded differently to the feedback uncertainty levels in their reliance on the expected shift. Although not significant in pairwise

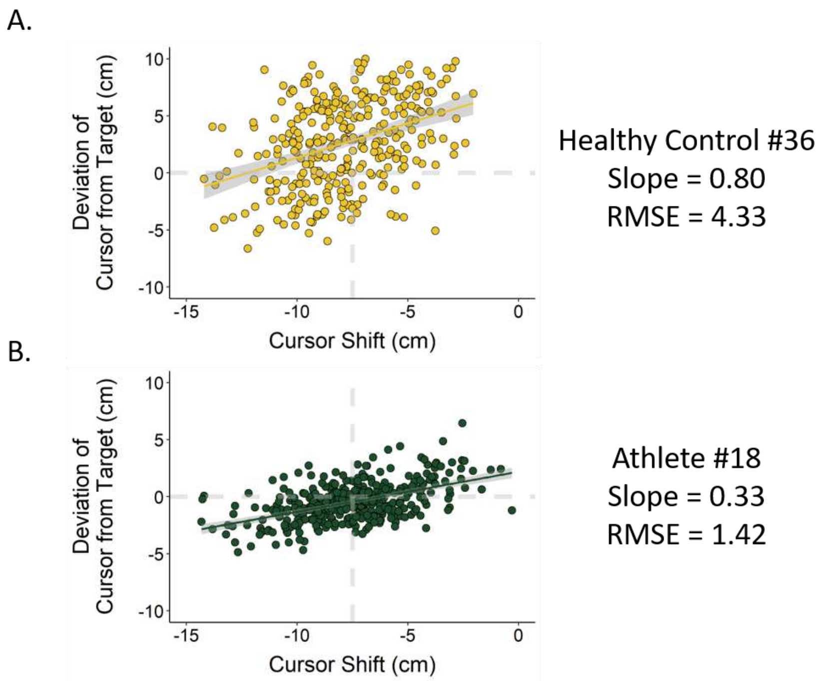


Figure 3.4. Two participants' data from the small feedback uncertainty condition. According to the Bayesian framework, the slope of the regression line should be close to zero in this condition indicating a greater reliance on the available sensory data and a small reliance on the expected shift. A. Data from participant #36 of the HC group. B. Data from participant #18 of the ATH group.

comparisons, Figure 3. 5.A shows that the ATH group relies less on the expected shift across the first three conditions than the other two groups and then relies completely on the shift in the complete uncertainty condition.

In addition, the one way ANOVA assessing differences in the Bayes values across the three groups showed a significant main effect for group ($F(2,53) = 3.56$, $p = 0.035$) and pairwise comparisons also found the ATH group to be significantly higher than the HC group ($p = 0.026$) but not the ACT group ($p = 0.515$) (Figure 3.6). Also, the ACT group was not significantly different than the HC group ($p = 0.286$). Taken together, these results confirm that the ATH group estimated their CoM positions during full body movement in a way that better fit the Bayesian framework when compared to the HC

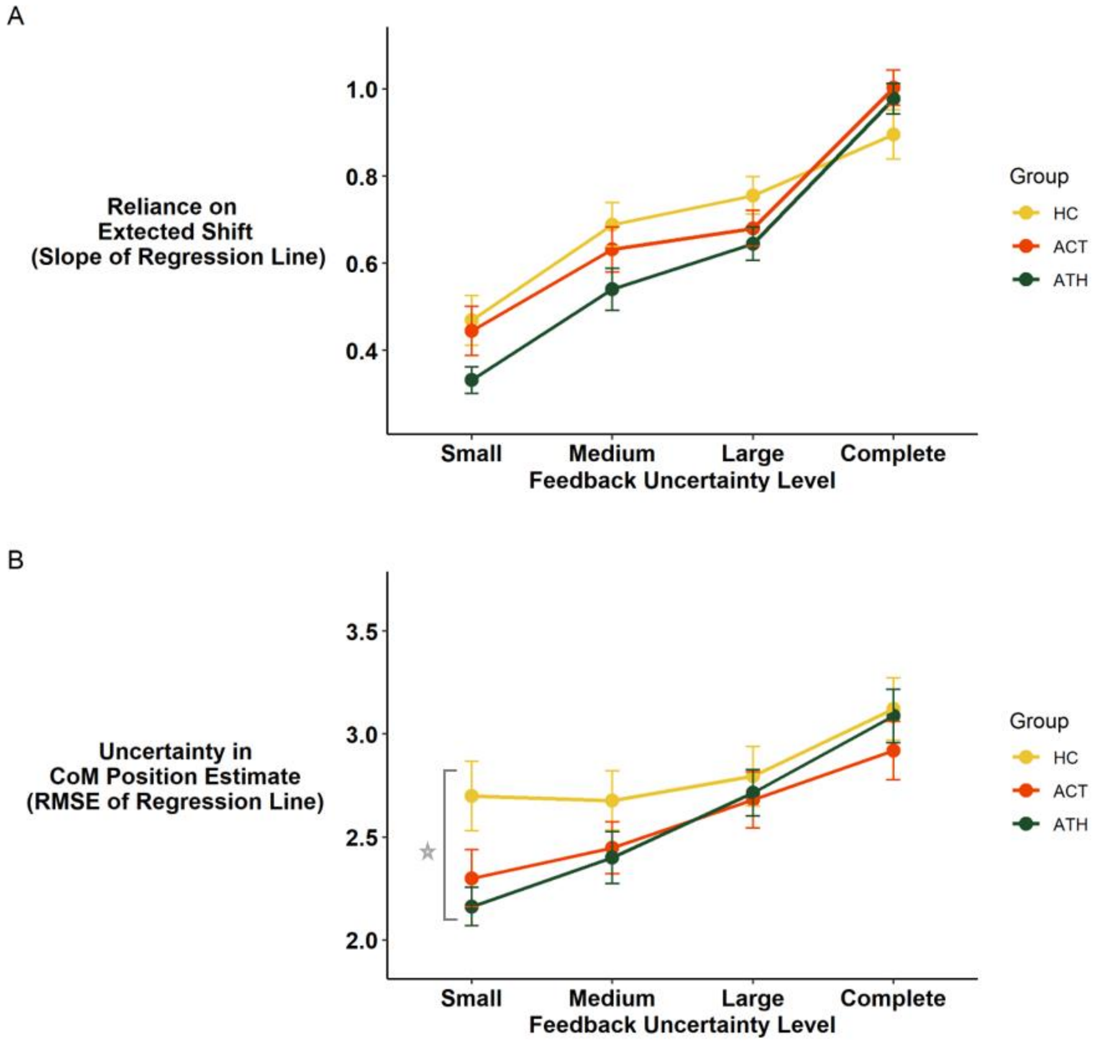


Figure 3.5. Plots for reliance on the expected shift and the uncertainty values across the four feedback uncertainty levels. A. I found a significant Group x Feedback Uncertainty Level interaction effect ($p = 0.012$) for the Reliance on the shift variable. B. I also found a significant Group x Feedback Uncertainty Level interaction effect for the response uncertainty variable ($p = 0.032$). Pairwise comparisons also showed a significant difference in uncertainty between the ATH group and the HC group when feedback uncertainty was low. ★= $p < 0.05$.

group. Furthermore, results suggest that the ACT group also fit the Bayesian framework better than the HC group though this was not found to be significantly different.

I also expected that the athletic group would demonstrate a smaller amount of uncertainty in their position estimates while performing the full-body mobility task. As a

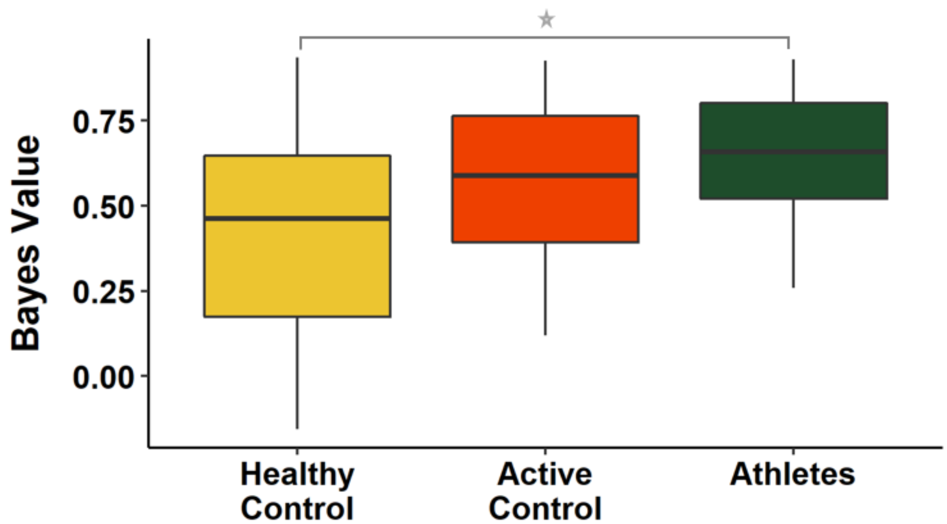


Figure 3.6. Bayes values for the three groups. A significant group effect was found from a one-way ANOVA ($p = 0.035$) and pairwise comparisons found the ATH group higher than the HC group. ★= $p < 0.05$.

reminder, I defined response uncertainty as the RMSE of the regression line of the linear fit between response accuracy and the cursor shift on each trial for each feedback uncertainty condition. Like the first hypothesis, I performed a three-way repeated measures ANOVA with random effects to identify differences across the three groups in their response uncertainty. Results from the repeated measures ANOVA identified a significant group by feedback interaction effect on response uncertainty ($F(6,159)= 2.36$, $p = 0.032$). Follow up pairwise comparisons with Tukey's honest significance test (Figure 3.5. B) indicated a significant difference of uncertainty between the ATH group and the HC group in the small feedback uncertainty level ($p = 0.015$).

Finally, to examine a difference in balance performance across the three groups I performed a three (group) by four (feedback uncertainty levels) repeated measures ANOVA on the VTC minima value described previously. The results of this ANOVA showed a significant main effect of group ($F(2,53)= 3.717$, $p = 0.031$) (Figure 3.7).

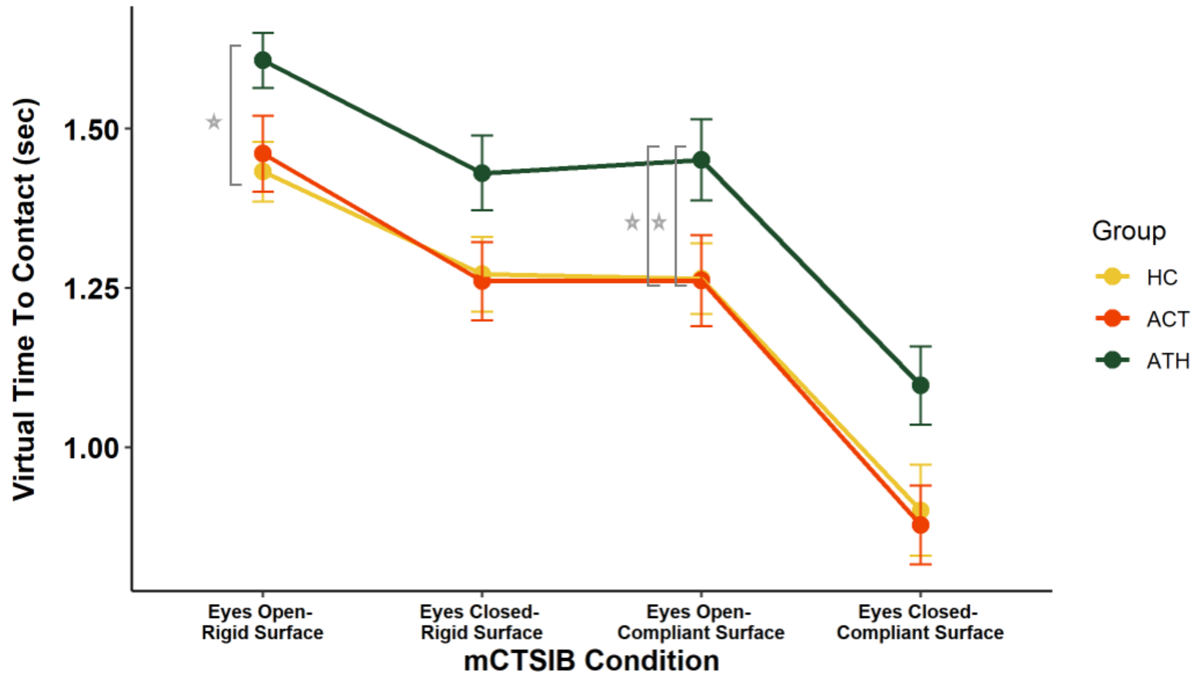


Figure 3.7. Balance results for all groups across the conditions of the mCTSIB. ★= p < 0.05.

Pairwise comparisons indicated a significant difference in VTC between the ATH group and the HC group in both the eyes open-rigid surface condition (p = 0.043) and the eyes open-compliant surface condition (p = 0.039). A significant difference was also found between the ATH group and the ACT group in the eyes open-compliant surface condition (p = 0.047). All other pairwise comparisons between groups were not significant.

Interestingly, when analyzing the balance data from all participants, I found that the athletes within the ATH group that played soccer performed much better than all other participants included in this study (Figure 3.8). They showed significantly higher VTC values than all other groups in the study in each of the four mCTSIB conditions (p < 0.05).

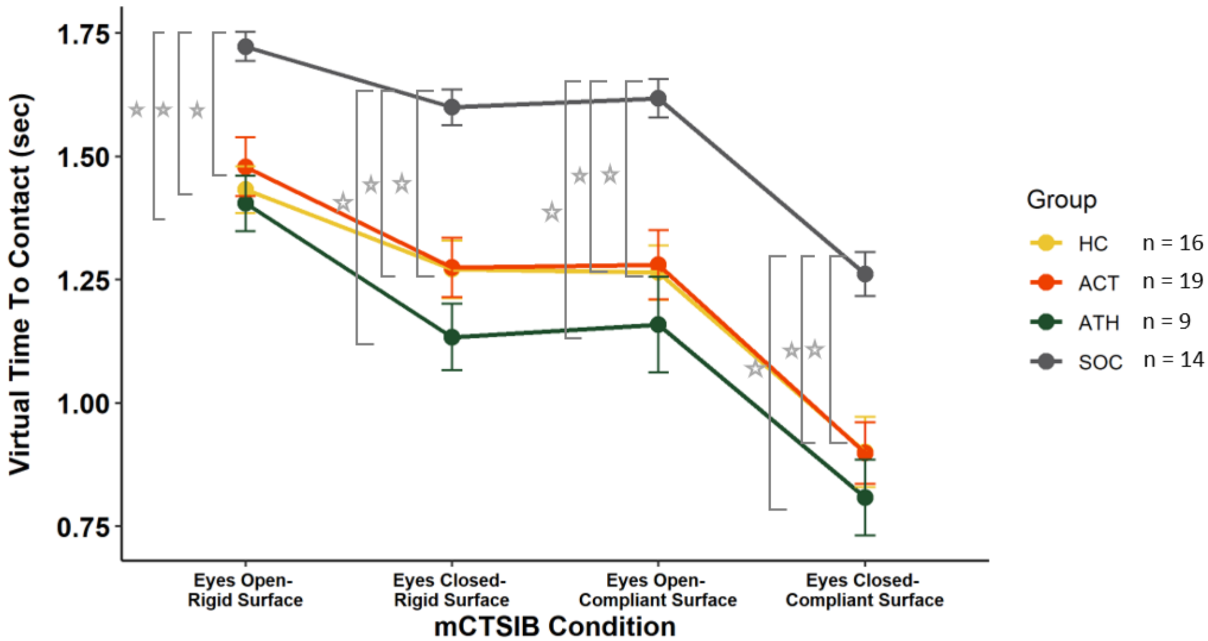


Figure 3.8. Balance results for all groups with the soccer athletes divided into their own group (SOC) and all other athletes making the ATH group. The SOC group was significantly better in all conditions than the other three groups. ★= $p < 0.05$.

Of interest, the other athletes included in this study actually performed worse than the ACT and HC groups although these were not found to be significant.

No associations between any of the Bayesian metrics and the balance performance measurements were found to be significant in the statistical analysis.

Discussion

The purpose of this study was to clarify if Bayesian inference in full body stepping movements is beneficial to overall mobility and balance performance. I found that the ATH group best fit the Bayesian model of body position estimation when compared to the ACT and HC groups. I also found that the ATH group estimated their positions with a smaller amount of uncertainty compared to the HC group. A main purpose of Bayesian inference is to minimize the amount of uncertainty when estimating an unknown parameter by combining the available evidence with previously acquired knowledge/data. These results indicate that elite athletes utilize Bayesian inference in their body position estimates, and that they do it in a more optimal way according to the Bayesian model. Though not statistically significant, I also showed that the physically active group (ACT) followed behind the ATH group in fitting the Bayesian model better than the HC group. These results add interesting clarity to the use of the Bayesian model in estimating body position and provide compelling evidence that physical activity aids in a person's ability to make Bayes optimal body position estimates. The following paragraphs will expound on these results, elaborate on their possible implications and set forth a few viable paths for future research on this topic.

I hypothesized that the ATH group would put more weight on their sensory information in scenarios where the available sensory information was more certain when compared to the non-athletic groups. These results confirmed this hypothesis and showed that the degree that participants relied on their sensory input in the first three feedback uncertainty levels was impacted by their athletic status and physical activity level. This difference in sensory weight may be due to the improved sensory acuity that often accompanies elite sport performance. Previous research by Han and others (Marie Fabre, Blouin, & Mouchnino, 2021; Han et al., 2014; Han, Anson, et al., 2015; Han, Waddington, Anson, & Adams, 2015; Muaidi, Nicholson, & Refshauge, 2009) has shown that proprioceptive acuity is heightened in athletes and actually correlates with the amount of competitive success an athlete has. Though I didn't measure sensory acuity directly in this study, the VTC results I collected from the balance performance indicate that the ATH group was better at handling challenging sensory conditions. Moreover, the finding that the ATH group had less uncertainty in their responses further confirms the hypothesis that the ATH group is superior at using sensory information to control balance related movements. Whether this advantage is attributed to the acquisition of sensory data less plagued with noise or a heightened ability to integrate and perceive uncertain sensory cues will be the focus of future research. Truthfully, it is likely a combination of both methods as they both have shown to be elevated in elite motor performers (Adkins, Boychuk, Remple, & Kleim, 2006; Fong & Ng, 2012; Johnson & Woollacott, 2011; Koceja, Davison, & Robertson, 2004; Vuillerme, Teasdale, & Nougier, 2001; Zehr, 2006).

Also, I found that the athletic group relied almost entirely on the learned expectation of CoM position in the complete feedback uncertainty condition. This finding does not come as a surprise when considering the numerous occasions that athletes must generate a movement in scenarios where sensory information is either uncertain or not temporally available to inform the movement parameters. In situations where an athlete must quickly respond to an external cue or perform a rapid motor skill, the resulting sensory data is not received by the CNS in enough time to inform a subsequent efferent signal. In these scenarios, an athlete's (or non-athlete performing a movement of a similar context) nervous system must control motor skills using predictions of body state based on previously attempted movements of a similar type (Flanagan et al., 2003; Shadmehr et al., 2010; Wolpert & Ghahramani, 2000). In these scenarios, an individual with the most accurate prediction of body dynamics is more likely to successfully execute the movement being performed. As follows, athletes generally have significantly more experience performing goal-oriented voluntarily generated motor skills that help to sculpt an accurate internal representation of their motor capabilities. These findings are in line with previous research showing that athletic performance helps to build accurate internal representations of one's body (Callan & Naito, 2014; Marie Fabre et al., 2021; Mouchnino, Aurenty, Massion, & Pedotti, 1992). This previous research may also shed light onto the finding that the HC group, that were more sedentary than the other groups, did not rely on the learned expectation of CoM position as well as the ATH group in the complete feedback uncertainty condition.

I found that athletes rely more on their sensory information in circumstances of uncertainty and that they are better at relying on learned expectations of body position when sensory information is unavailable. These findings can be applied in many ways. One possible area of applying these findings would be to emphasize the benefit of promoting sensory acuity in all populations. There is a vast body of successful research on improving sensory function in healthy and clinical populations (Alexandre de Assis, Luvizutto, Bruno, & Sande de Souza, 2020; Aman et al., 2014; Lorach, Marre, Sahel, Benosman, & Picaud, 2013). Additionally, the findings from this study and past research (Herpin et al., 2010; P. Perrin, Deviterne, Hugel, & Perrot, 2002; P. P. Perrin, Gauchard, Perrot, & Jeandel, 1999) suggest that physical activity can be effective at improving proprioception in both old and young people. Along with the need to improve sensory acuity in all populations, I also found that working to improve movement expectations can be effective at improving motor function. Fabre and colleagues (2021) found that dance and sport training can effectively improve internal body representations and improve mobility in many populations. Additionally, Fabre et al. (2020) showed that a rehabilitative intervention aimed at improving the internal body representation of obese patients helped to improve balance in this population without losing weight. These results are promising when considering that movement predictions are gradually more important as sensory information becomes less certain. Also, in clinical populations when sensory input is directly affected, an impaired ability to predict movement dynamics can lead to harmful motor errors (Arpin et al., 2017).

The athletic group in this study also performed significantly better in the balance assessment than the HC group. The advantages of athletic participation on balance performance have been consistently reported in previous research (Hammami, Behm, Chtara, Ben Othman, & Chaouachi, 2014; Muaidi et al., 2009). Interestingly, a post-hoc analysis identified the soccer athletes as the group with superior balance control compared to all other participants in the study. Bressel and colleagues (2007) also found soccer athletes to have superior balance when compared to other sports. This may be due to the nature of the sport of soccer in comparison to the other sports included in this study. Soccer is a very dynamic sport that likely demands greater variability and adaptability in one's motor toolbox. These demands may foster the development of sensory abilities that benefit balance and mobility better than other sports. Hammami and colleagues (2014) also found that athletes involved in a sport that included in-motion regulatory conditions had better balance than athletes in sports with stationary regulatory conditions.

This study was among the first to translate the vast body of research on Bayesian inference in motor control to a different population with the purpose of understanding and improving motor function. Vilares et al. (2017) used the Bayesian model to measure the degree that patients with Parkinson's disease relied on their sensory information while on and off of dopaminergic medication. Combined with the work of Vilares et al. (2017) I showed that the Bayesian model of understanding sensory uncertainty can be used to measure motor performance and that individuals who more ideally fit the model are at an advantage in performing motor skills.

Interestingly, I found no correlation between the Bayesian measurements of reliance on the expected CoM position or uncertainty with the balance measurements included in this study. As previously mentioned, athletes clearly performed better in both assessments but the lack of association between the two suggests that, although both involved with mobility and balance related skills, may be controlled by different neural mechanisms. Hrysomallis et al. (2006) found that young healthy individuals performed well in both static and dynamic balance assessments, but the two metrics showed only weak associations. The virtual reality protocol involved stepping in multiple directions to move the CoM to varying targets. It may be that the ability to maintain static balance under challenging conditions requires different perceptual processes than stepping to move the CoM to visual targets. Stevenson and colleagues (2009) showed that the center of pressure is estimated in a Bayesian way in a one-dimensional balance task. The way these two mobility related motor skills differ in handling sensory uncertainty will be the focus of future research.

This study involved a few limitations that restrict the area of application for the resultant findings. First, I only included females in this study. One of the main purposes of the study was to assess the Bayesian model of motor control in individuals with superior balance and motor control and because athletes and women have both shown to perform better in balance and mobility, I included only females in this study (Goble et al., 2019). Also it would have been advantageous to have equal representations of all sports in the athletic group however, scheduling and available sports teams to recruit were limited to the athletes included in this study. Finally, I used self-reported physical activity levels to delineate between the active control group (ACT) and the healthy control group (HC). Although self-reported physical activity is not an ideal way to measure physical fitness levels, previous work has shown it to be an effective way to measure physical activity in a young healthy population (Nelson, Taylor, & Vella, 2019).

To conclude, I assessed the Bayesian model of sensory uncertainty in a full-body stepping movement in three different populations. I found that the athletic population fit the model best and that the non-physically active control group fit the Bayesian model least. These results add to a large body of research to understand how sensory uncertainty is handled by the CNS. I also showed that the Bayesian model of motor control can be used to assess how sensory information is being used in any population. This provides an additional method to measure the efficacy of rehabilitative practices aimed at improving sensory function. Overall, I found that individuals are at an advantage if they make Bayes optimal body position estimates which will ultimately help them in mobility related motor tasks.

CHAPTER 4 – BAYESIAN INFERENCE REVEALS DECREASES IN SENSORIMOTOR UNCERTAINTY RESULTING FROM TENS

Introduction

Balance and mobility are fundamental contributors to independent living throughout the lifespan. Walking ability is an important predictor of quality of life in multiple populations (Gunn, Creanor, Haas, Marsden, & Freeman; Neufeld, Machacova, Mossey, & Luborsky), whereas poor mobility leads to decreased quality of life, falls, and often harmful injuries. In adults over the age of sixty-five, falls are the leading cause of fatal and non-fatal injuries (WISQARS). This is particularly troubling as is it predicted that by 2030, older adults will outnumber children for the first time in U.S. history (Bureau, Accessed February, 2020). Therefore, much research has endeavored to develop effective rehabilitative practices to mitigate, or even eliminate, mobility impairments in aging and neurodegenerative populations (Baird, Sandroff, & Motl, 2018; Melese, Alamer, Hailu Temesgen, & Kahsay, 2020; Zhang, Low, Gwynn, & Clemson, 2019).

One therapeutic approach that has shown to be an effective method to improve mobility in clinical populations is the use of electrical stimulation of muscle groups used in gait and balance (Enoka, Amiridis, & Duchateau, 2020). Of the many ways to apply stimulation to muscle fibers in the periphery, transcutaneous electric nerve stimulation (TENS) is a relatively new approach to improving sensorimotor function that has shown promising results (Almuklass, Capobianco, Feeney, Alvarez, & Enoka, 2020; Elboim-Gabyzon et al., 2019; Kwong et al., 2018). TENS has historically been used in other realms of physical health to manage pain (Resende et al., 2018) and muscle spasticity

(Ping Ho Chung & Kam Kwan Cheng, 2010), but has recently been applied to improve gait and balance in various populations (Almuklass et al., 2020; Elboim-Gabyzon et al., 2019; Enoka et al., 2020; Kwong et al., 2018). TENS is a method of electrical stimulation in which the applied current is targeted directly at sensory nerve fibers. When applied to improve sensorimotor function of mobility, electrodes are placed on the muscles of the lower limbs and the applied current is set at a level below the motor threshold, to minimize any evoked muscle contractions. Used in this way, action potentials in several sensory receptors are elicited both in and around the targeted muscle (Rangwani & Park, 2021; Zéronian, Noé, & Paillard, 2021).

Recent research has found that, when used concurrently with clinical metrics of mobility and motor function, TENS improves performance when compared to the same metric without the addition of TENS (Almuklass et al., 2020; Elboim-Gabyzon et al., 2019; Kwong et al., 2018). Almuklass and colleagues (2020) applied continuous asymmetrical biphasic pulses (0.2 ms) at a rate of 50 Hz just below the motor threshold for both people with MS as well as age-matched controls as they performed various metrics of overall sensorimotor function. Almuklass et al. (2020) found that both groups (MS and controls) improved in the 6-minute walk test and the MS group also improved in a timed chair rise test when compared to performing with no TENS. Additionally, Elboim-Gabyzon et al. (2019) showed that patients recovering from hip surgery walked further during a 2-minute walk test when receiving TENS than a group that received no stimulation. Finally, in a review article including 11 studies and 439 stroke survivors, Kwong et al. (2018) concluded that TENS is beneficial to walking and mobility and improves patients' walking capacity.

While there is ample evidence of the benefit that TENS has on gait and mobility, the underlying mechanisms that lead to these improvements are not understood. As mentioned previously, the amplitude of TENS is often set at a level below the motor threshold, i.e., the minimal intensity of stimulation that generates an involuntary motor response (Zéronian et al., 2021). Thus, the argument that any benefit comes from direct excitation of additional muscle activation is unlikely. TENS has generally been applied as a way of sensory augmentation where the applied electric current elicits additional sensory information that conveys pertinent information about body orientation (Sienko et al., 2018). Recent work has provided evidence that sensory input has a much larger impact on overall motor function than has previously been understood (Gesslbauer et al., 2017; Kumar et al., 2019; Mirdamadi & Block, 2020, 2021; Ostry & Gribble, 2016). Thus, the observed benefits in gait and mobility that result from the use of TENS may be due to increased sensory input relaying additional information about body orientation. However, it is not clear how the additional information is used by the central nervous system to inform body position awareness or construct motor plans. One hypothesis is that the additional sensory input decreases the total noise in the incoming sensory data leading to less uncertainty in the central nervous system's (CNS) estimation of body orientation. If this were the case, the observed benefits that accompany the use of TENS would be due to improved positional awareness leading to more efficient motor plans. Though this hypothesis seems conceptually valid, identifying a way to measure and quantify it requires robust assessment.

Bayesian inference is a statistical model that has been used to identify an unknown parameter when the available data is clouded with uncertainty (Bayes, 1763; Kording &

Wolpert, 2004a). Simply put, Bayesian inference posits that the most likely estimate of an unknown parameter comes by combining the available data with previously collected data. The variability of either dataset determines the influence that it will have on the final estimate. Specific to the context of motor control, this suggests that the most likely estimate for the location of a body part is calculated by considering the mean and variability of both the recent sensory information as well as the expected location of the body part despite the current sensory data. Past research has shown that the CNS calculates body position in a way consistent with Bayesian inference (Kording & Wolpert, 2004a, 2006). Additionally, I have shown in previous chapters that the CNS estimates the position of the center of mass (CoM) during full body stepping movements in a way consistent with Bayesian inference. What's more, I also provide evidence in previous chapters that individuals with superior mobility capabilities estimate the position of their CoM with less uncertainty in the same movement. Using the Bayesian methods in a novel way, I hope to expose some of the underlying perceptual mechanisms that benefit with the addition of TENS on the lower extremities during mobility related movements.

The purpose of this study was to clarify the underlying mechanisms that lead to the benefits of using TENS to improve gait and mobility. Using the model of Bayesian inference in motor control, I expected that participants would display less uncertainty when estimating the position of their CoM during a mobility related movement. Furthermore, I expected that participants would rely more on sensory cues and less on the learned expectation of their CoM position when receiving TENS. Finally, I hypothesized that participants would also display better static balance when receiving TENS than without TENS.

Methods

Participants

A total of 31 young adults participated in this study (age range: 19-33 years, 18 female). One participant suffered a musculoskeletal injury in between study visits and was excluded from the analysis. As a result, 30 participants were included in the final analysis. All participants were pseudo-randomly assigned to one of three study groups (accounting for balanced representations of male/females). Group NN (no TENS/no Tens) received no TENS stimulation on either of their study visits. Group NT (no TENS/TENS) received TENS stimulation on only their second visit. Group TN (TENS/no TENS) received TENS stimulation on their first visit only. All participants were healthy with no serious injuries or ailments limiting their physical abilities. A complete description of participant and group demographics and characteristics can be found in Table 4.1.

Table 4.1. Group Demographics and Characteristics

Group	NN	NT	TN	p – value*
n	10	10	10	
Sex: Male (%)	4 (40.0)	4 (40.0)	5 (50.0)	0.873
Age: Years (mean (SD))	23.40 (2.17)	24.70 (4.00)	23.80 (3.39)	0.666
Height: Inches (mean (SD))	67.75 (3.79)	67.80 (4.45)	68.60 (3.05)	0.855
Weight: Pounds (mean (SD))	163.80 (37.55)	161.10 (35.33)	171.40 (31.03)	0.791
BMI: Kg/M^2 (mean (SD))	24.96 (4.02)	24.41 (3.49)	25.64 (4.40)	0.788
Exercise: Min/week (mean (SD))	318.89 (202.00)	394.00 (219.91)	343.75 (103.45)	0.657

NN= No TENS/No TENS, NT = No TENS/TENS, TN = TENS/No TENS.
* p values represent the significance level from a group effect in a one-way ANOVA with each respective variable as the response variable

Study Protocol

As mentioned above, participation involved two visits to the laboratory where they completed the same protocol on each visit (Figure 4.1) with the only differences being whether they received TENS. Following the consent process on their first visit (and

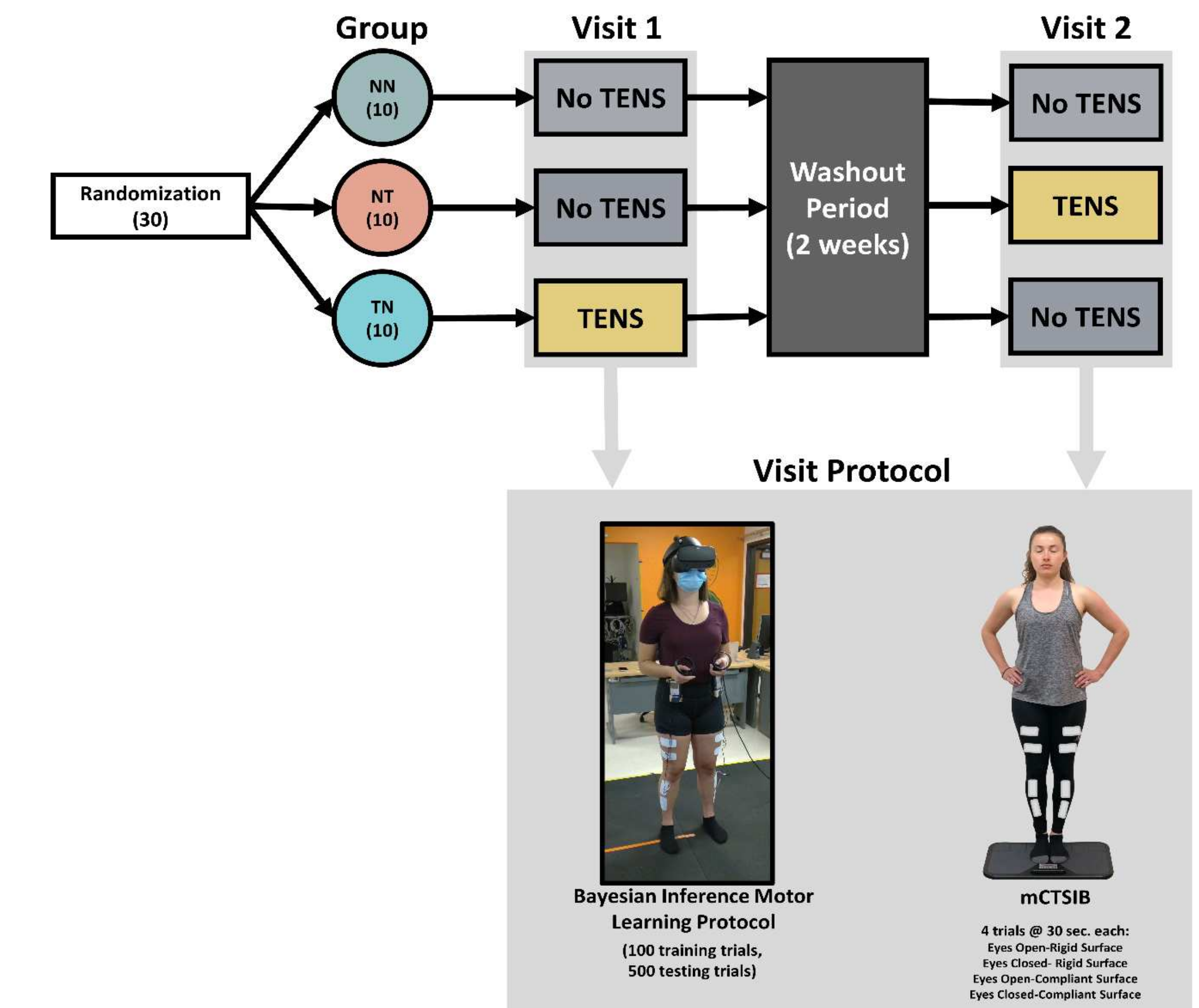


Figure 4.1. Study Design and Protocol. Thirty healthy young participants were pseudo-randomly assigned to one of three study groups. The NN group received no TENS stimulation on either visit. The NT group received TENS stimulation only on their second visit. The TN group received TENS stimulation on their first visit. All participants visited the lab twice and completed the same protocol on each visit. Visit protocol involved completion of a motor learning protocol performed in virtual reality as well as completion of the modified clinical test of sensory integration for balance (mCTSIB).

immediately upon entering the lab on their second visit), the TENS electrodes were placed over the distal and proximal end of the vastus lateralis and tibialis anterior of both legs with the cathode placed at the distal end (Figure 4.1). Participants first completed the modified clinical test of sensory integration for balance (mCTSIB) (refer to chapter 3 for details on the mCTSIB) followed by set up and completion of the Bayesian inference motor learning protocol performed in virtual reality (refer to chapter 2 for details on the motor learning assessment).

TENS Protocol

Following similar methods of Almuklass et al. (2020), the TENS intervention was applied with an FDA-approved clinical TENS device LG-TECELITE Therapy System (LGMedSupply, Cherry Hill, NJ). Stimulation involved continuous asymmetrical biphasic pulses delivered with electrode pairs (2 in. X 4 in. pads) placed on the skin over the vastus lateralis and tibialis anterior muscles of both legs. Stimulus frequency was set at 50 Hz with pulse width of 0.2 ms. The area over the skin was shaved to minimize electrical impedance for all participants. Electrodes were placed at the same locations on both visits, but a current was only delivered on the appropriate visit according to their group designation. Amplitude of TENS stimulation varied for each participant and was determined by their specific motor threshold. To identify the motor threshold for each participant, TENS amplitude was slowly increased at 1 mA increments on each individual muscle until non-voluntary muscle contractions could either be seen or felt by the researcher. The TENS amplitude used during assessments was 2 mA below the motor threshold for each muscle and limb (Almuklass et al.). During the assessment, the TENS was only applied while the assessment was being performed and was not applied in between blocks and assessments.

Analysis

Data Analysis

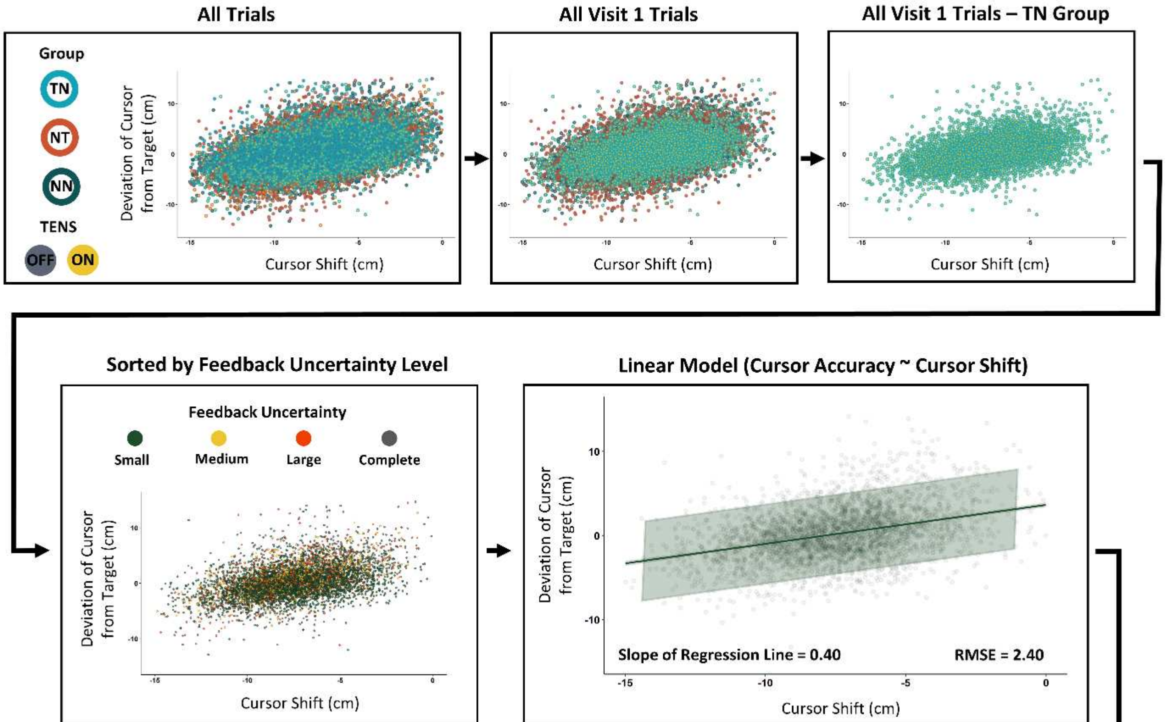
Analysis of the Bayesian motor learning assessment data from each group and participant was analyzed in two different ways. The first way (referred from here on as the "participant level") was consistent with what has been done in chapters 2 and 3 (refer to chapter 2/Figure 2.2 for a full description). In this way, the 600 trials performed by a participant on one study visit are reduced to 8 values: 4 values for the slope of the regression line between the cursor shift and their cursor accuracy for each feedback uncertainty condition and 4 values for the RMSE of each of those regression lines. As a reminder, the slope of the regression line is used as a measurement of how much the expected cursor shift impacted their final position estimate. A slope closer to zero would indicate that the shift had little impact on their response, and they relied more on the sensory input that they received. A slope closer to one would indicate a greater reliance on the expected shift when estimating the cursor position (the position of their CoM). The RMSE is used to measure the response uncertainty of the participant as they are required to estimate their cursor position with limited sensory input. A smaller value represents less uncertainty in their responses/more confidence in the responses that they make. A higher value represents the opposite: more uncertainty in their responses/less confidence in the responses they make.

The second way that the data from the motor learning assessment was assessed was by including all trials performed by all participants in the analysis (referred from here on as the "trial level"). In this study, thirty participants performed six hundred trials on two separate visits to the lab. That resulted in roughly 36,000 trials performed for this project. For the trial analysis, the total trials performed were partitioned depending on the visit, group, TENS condition, and feedback uncertainty level. From there, a linear model for each partitioned dataset was calculated with the cursor shift as the predictor variable and the cursor accuracy (distance of the cursor from the target) as the response variable. The model parameters were then used in further analysis to identify differences between visits/groups/TENS conditions (Figure 4.2). In the trial level of analysis, all trials completed in the study are included in the analysis.

Analysis of the balance performance data was done using the virtual time-to-contact measurement that was used in chapter 3. Virtual time-to-contact (VTC) considers the instantaneous position, velocity and acceleration of the center of pressure (CoP), to predict how long it would take the CoP to reach the boundary of the base of support for every data point in a trial. A lower VTC value means that it would take less time to reach the boundary of the base of support and subsequently fall, thus exemplifying a state of low stability. Details on the calculation of the VTC variable can be found in chapter 3.

Statistical Analysis

All statistical analysis was conducted in R software (version 4.1.1) with an alpha level set at 0.05. To ensure statistical assumptions were met prior to running any statistical tests, assessments of normality and equality of variance were performed on all outcome metrics of this study such as: Levene's test for equality of variance, A.



B.

Group	Visit	Condition	TENS	Slope (β_1)	RMSE	F	DF_1	DF_2	r^2	p
TN	***1***	***Small***	***ON***	***0.40***	***2.40***	***609.88***	***1***	***3583.28***	***0.19***	***1.76E-124***
NT	1	Small	OFF	0.49	2.64	753.85	1	3649.13	0.29	4.97E-151
NN	1	Small	OFF	0.47	2.70	660.45	1	3628.70	0.23	5.88E-134
TN	1	Medium	ON	0.63	2.31	338.56	1	776.72	0.35	4.96E-63
NT	1	Medium	OFF	0.69	2.85	267.71	1	746.29	0.49	1.19E-51
NN	1	Medium	OFF	0.72	2.56	372.38	1	746.95	0.36	1.25E-67
TN	1	Large	ON	0.73	2.68	347.08	1	763.62	0.41	3.84E-64
NT	1	Large	OFF	0.76	3.02	301.48	1	755.48	0.54	4.42E-57
NN	1	Large	OFF	0.74	2.71	345.99	1	785.41	0.34	2.87E-64
TN	1	Complete	ON	0.91	2.97	452.72	1	760.94	0.47	3.43E-79
NT	1	Complete	OFF	1.02	3.12	483.08	1	739.96	0.49	8.44E-83
NN	1	Complete	OFF	1.02	2.94	546.08	1	752.76	0.48	3.07E-91
TN	2	Small	OFF	0.31	1.77	719.46	1	3701.48	0.23	5.58E-145
NT	2	Small	ON	0.46	2.02	1154.15	1	3621.49	0.33	7.59E-220
NN	2	Small	OFF	0.40	2.19	785.71	1	3598.41	0.20	1.50E-156
TN	2	Medium	OFF	0.61	2.06	440.53	1	826.72	0.49	9.82E-79
NT	2	Medium	ON	0.75	2.20	513.42	1	761.24	0.53	2.80E-87
NN	2	Medium	OFF	0.69	2.52	353.30	1	789.82	0.35	1.99E-65
TN	2	Large	OFF	0.68	2.23	462.17	1	768.26	0.55	1.25E-80
NT	2	Large	ON	0.84	2.48	528.64	1	765.49	0.57	2.36E-89
NN	2	Large	OFF	0.75	2.72	347.57	1	777.73	0.34	2.09E-64
TN	2	Complete	OFF	0.96	2.48	770.61	1	813.19	0.64	7.76E-120
NT	2	Complete	ON	1.00	2.57	664.41	1	761.76	0.55	7.80E-106
NN	2	Complete	OFF	1.04	2.73	671.83	1	767.13	0.50	6.94E-107

Figure 4.2. Analysis and results of data at the trial level. A. The total trials performed in the study were sorted into specific conditions based on study visit, group, and feedback uncertainty level. B. For each partitioned dataset, a linear model was calculated, and characteristics of each model are listed above. The slope (β_1) value is used to measure reliance on the cursor shift and RMSE is used to measure the amount of uncertainty in participants' responses.

Shapiro-Wilk tests, QQ plots and plots of the residual vs. fitted data. These assessments indicated that all the outcome metrics used in this study met the assumptions needed and were included in further analysis.

The first hypothesis for this study was that, according to the model of Bayesian inference in motor control, participants would display less uncertainty when estimating the position of their CoM during a mobility related movement while receiving TENS. This was assessed in two different ways. At the participants level, to assess differences in uncertainty between visits and research groups, a three (groups) by two (research visits) repeated measures ANOVA was calculated with random effects to account for each participant being represented by more than one observation within the analyzed data (four values of uncertainty across the feedback uncertainty conditions). To identify specific differences between groups and visits, follow up pairwise comparisons were calculated using Tukey's honest significance test. The second way that I assessed the first hypothesis was at the trial level. For this analysis, I calculated a separate linear model for each visit, group, and feedback uncertainty condition, also with random effects to account for the variability inherent to each participant (Figure 4.2). In this analysis, differences in uncertainty between models can identify the effect of TENS.

Furthermore, I expected that participants receiving TENS would rely more on sensory cues and less on the learned expectation of their CoM position when compared to the same movements performed without TENS. Like the first hypothesis, this was assessed in two separate ways. At the participants level, to assess differences in sensory reliance between visits and research groups, a three (groups) by two (research visits) repeated measures ANOVA was calculated with random effects to account for each participant being represented by more than one observation within the analyzed data (four values of sensory reliance across the feedback uncertainty conditions). To identify specific differences between groups and visits, follow up pairwise comparisons were calculated using Tukey's honest significance test. The second method of analysis was at the trial level. For this analysis, I calculated a separate linear model for each visit, group, and feedback uncertainty condition, also with random effects to account for the variability inherent to each participant (Figure 4.2). In this analysis, differences in the slope of the regression line between the cursor shift and cursor accuracy between models can identify the effect of TENS.

Finally, I hypothesized that participants would display better static balance when receiving TENS than without TENS. To address this hypothesis, a three (groups) by two (research visits) repeated measures ANOVA was calculated with random effects to account for each participant being represented by more than one observation within the analyzed data (four values of VTC across the sensory conditions of the mCTSIB). To identify specific differences between groups and visits, follow up pairwise comparisons were calculated using Tukey's honest significance test.

Results

In total, 30 neurotypical healthy adult participants were included in the final analysis. Characteristics of all study participants and groups are presented in table 4.1.

Participant Level Analysis

To assess differences in the uncertainty of participants' responses across study visits and groups, I performed a three by two repeated measures ANOVA with random effects. The results of that ANOVA showed a significant main effect for visit ($F(1,207)= 37.28$, $p < 0.001$) indicating that response uncertainty, on average across all participants irrespective of group, decreased from visit 1 to visit 2 (Figure 4.3 A). Additionally, I found a significant visit by group interaction effect ($F(2,207)= 3.29$, $p = 0.039$) indicating that the change in uncertainty across visits was not the same for each group. Follow up pairwise comparisons indicated that the groups that received TENS both significantly decreased in their response uncertainty from visit 1 to visit 2 ($p < 0.001$). However, the group that received no TENS on both visits did not significantly reduce their response uncertainty ($p = 0.108$). These results corroborate the first hypothesis that TENS would decrease the uncertainty in participants' estimates for where they were in space.

I also expected that TENS would result in participants relying more on the sensory input they received and less on the learned expectation of CoM position. This would be measured by a decrease in the slope of the regression line between cursor shift and cursor accuracy. The results of the three by two repeated measures ANOVA with random effects indicated no significant main effect for visit ($F(1,207)= 0.0001$, $p = 0.992$) and also no significant visit by group interaction effect ($F(2,207)= 0.140$, $p = 0.869$) (Figure 4.3 B). These results failed to reject the null hypothesis that their was no difference in the slope value across groups or visits and no effect of TENS.

Finally, I hypothesized that TENS would result in participants performing better in a static test of balance. This would be measured by an increase in the VTC measurement when TENS was applied compared to when TENS was not applied. The results of the three by two repeated measures ANOVA with random effects indicated no significant main effect for visit on the VTC measurement ($F(1,207)= 0.473$, $p = 0.492$) and also no

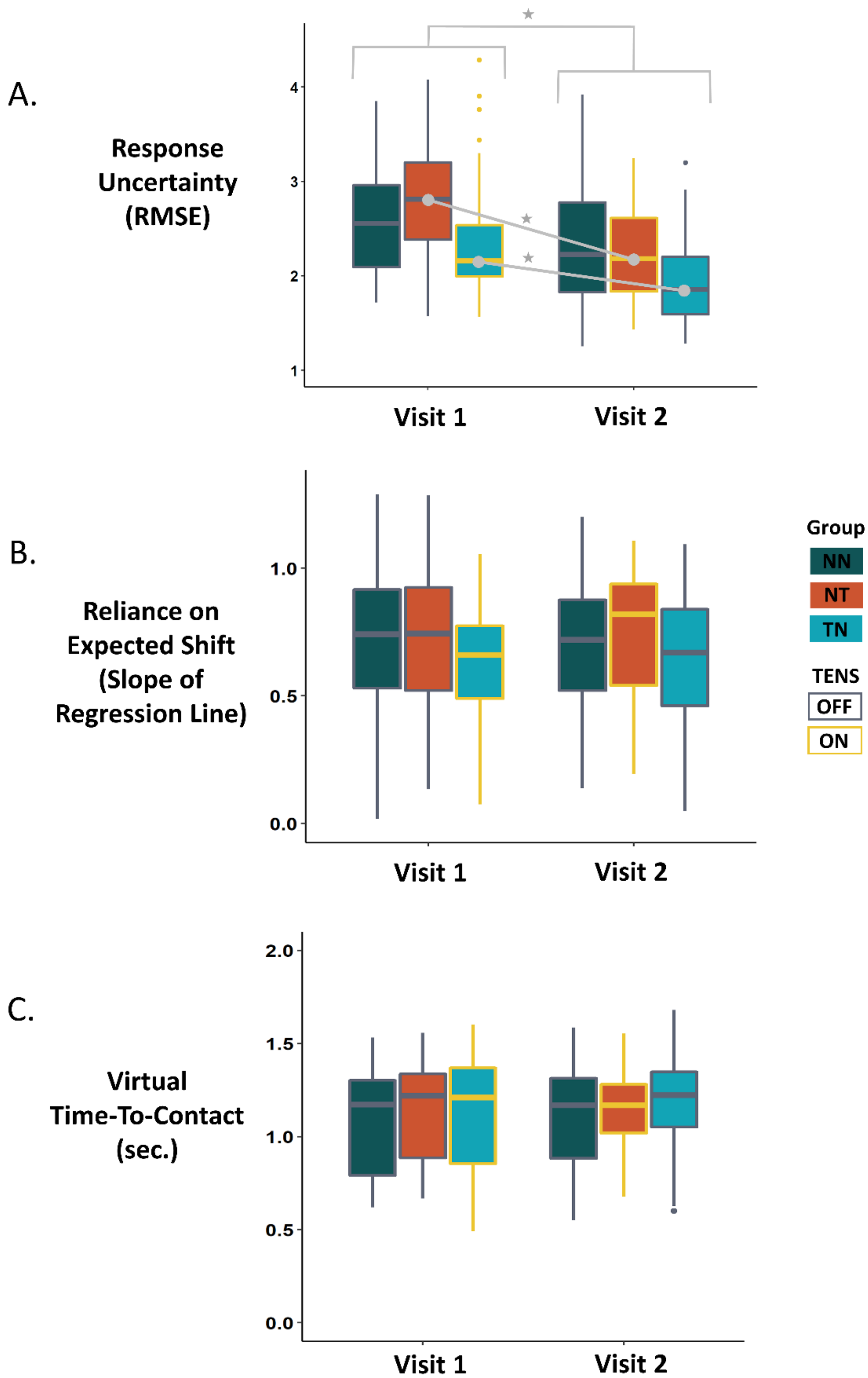


Figure 4.3. A. Response uncertainty for the three groups across visits. B. Reliance on the expected shift across visits. C. Virtual time-to-contact across study visits. Significant differences were only found in the response uncertainty metric across visits. The groups that received TENS significantly decreased their response uncertainty from visit to visit 2. ★= p value < 0.001.

significant visit by group interaction effect (F(2,207)= 0.135, p = 0.874) (Figure 4.3 C). These results failed to reject the null hypothesis that their was no difference in the VTC value across groups or visits and no effect of TENS.

Trial Level Analysis

In addition to assessing the first two hypotheses at the participant level, I performed further analysis with a higher granularity at the trial level. To accomplish this, I sorted all participants' trials into various subsets depending on the study visit, group, and feedback uncertainty level. Figures 4.4-8 illustrate the results of these analyses. Also, the specific parameters and results of each regression model can be found in figure 4.2. The first step of the trial level of analysis was to assess differences between visits for each group individually.

Group NN

Figure 4.4 shows the results from group NN across study visits. This group received no TENS on either visit. On both visits, their reliance on the expected shift

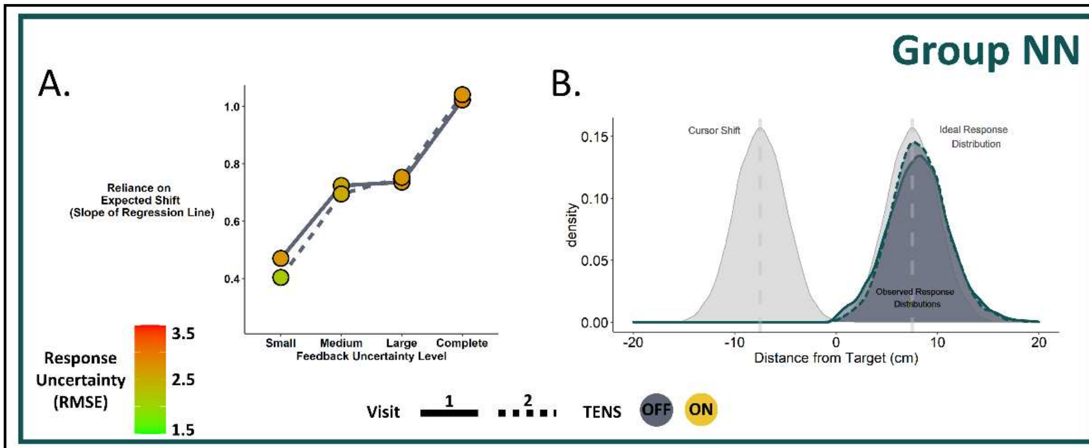


Figure 4.4. Trial analysis for group NN (received no TENS on either visit) across study visits. A. Reliance on expected shift and response uncertainty across feedback uncertainty levels. B. Response distributions of Group NN's responses for each visit compared to the distribution of cursor shift and ideal response distribution.

increased as feedback uncertainty increased. However, there was little difference for this reliance between visits except in the small feedback uncertainty condition where reliance on the shift appears to decrease from visit 1 to visit 2. Similarly, the response uncertainty (demonstrated by color in figure 4.4 A) appears to increase across feedback uncertainty conditions with little difference between visits except in the small feedback uncertainty condition where response uncertainty decreased in visit 2. Taken together, performance between visits in the group that received no TENS was very similar except in the small feedback uncertainty condition.

Group NT

Figure 4.5 shows the results from group NT across study visits. This group received no TENS on their first visit and TENS on their second visit. Similar to what has been shown previously, their reliance on the expected shift increased as feedback uncertainty increased on both visits. Also, there was little difference in reliance on the expected shift in the small and complete feedback uncertainty conditions, but an increase

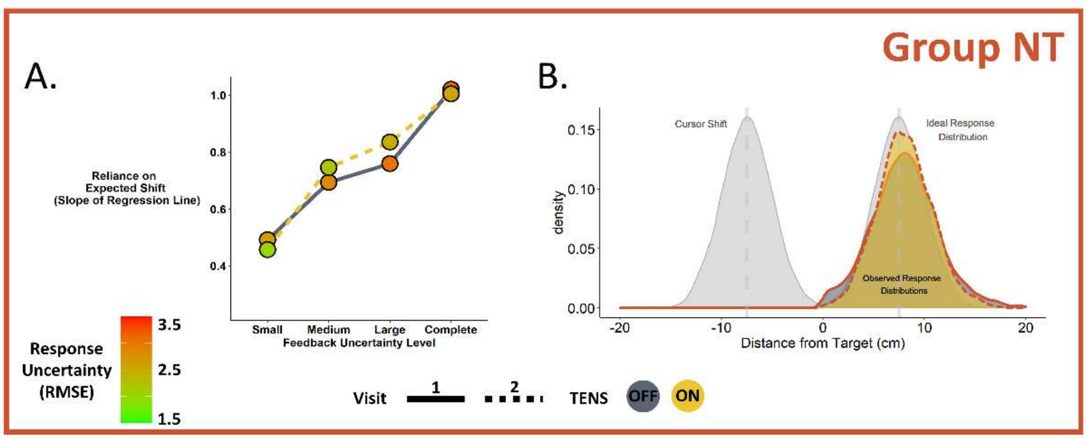


Figure 4.5. Trial analysis for group NT (received no TENS on their first visit and TENS on their second visit) across study visits. A. Reliance on expected shift and response uncertainty across feedback uncertainty levels. B. Response distributions of Group NT's responses for each visit compared to the distribution of cursor shift and ideal response distribution.

in reliance in the medium and complete feedback uncertainty conditions on their second visit when they received the TENS. With regards to the response uncertainty, it was decreased in visit 2 across all feedback uncertainty conditions when they received the TENS. Taken together, participants in the NT group appear to rely similarly on the expected shift, if not more so in certain scenarios with TENS, but are more confident in the responses that they make while receiving TENS.

Group TN

Figure 4.6 shows the results from group TN across study visits. This group received TENS on their first visit and no TENS on their second visit. Like what has been shown previously, their reliance on the expected shift increased as feedback uncertainty increased on both visits. Their reliance on the expected shift decreased from visit 1 to visit 2 in the first three feedback uncertainty conditions and increased in the complete feedback uncertainty condition. Similar to group NT, response uncertainty decreased from visit 1 to visit 2 across all feedback uncertainty conditions. Interestingly, their

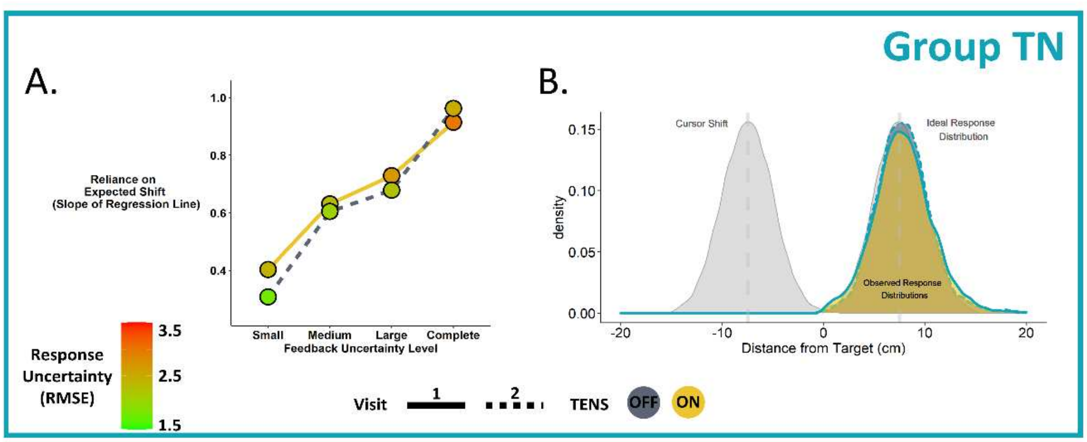


Figure 4.6. Trial analysis for group TN (received TENS on their first visit and no TENS on their second visit) across study visits. A. Reliance on expected shift and response uncertainty across feedback uncertainty levels. B. Response distributions of Group TN's responses for each visit compared to the distribution of cursor shift and ideal response distribution.

response distribution in visit 1 where they received TENS is very close to the ideal response distribution and then in visit 2 is almost identical to the ideal distribution. Taken together, participants that received TENS in the first visit, relied more on their sensory input and showed less response uncertainty when estimating their body position in their second visit where they received no TENS.

Visit 1

The next step in the trial level analysis was to assess differences between groups on each study visit. Figure 4.7 shows the results from all trials in visit 1. Figure 4.7 A shows a scatterplot of all trials from all participants identified by color. Figure 4.7 B shows the response distributions for all three groups on visit one compared to the distributions

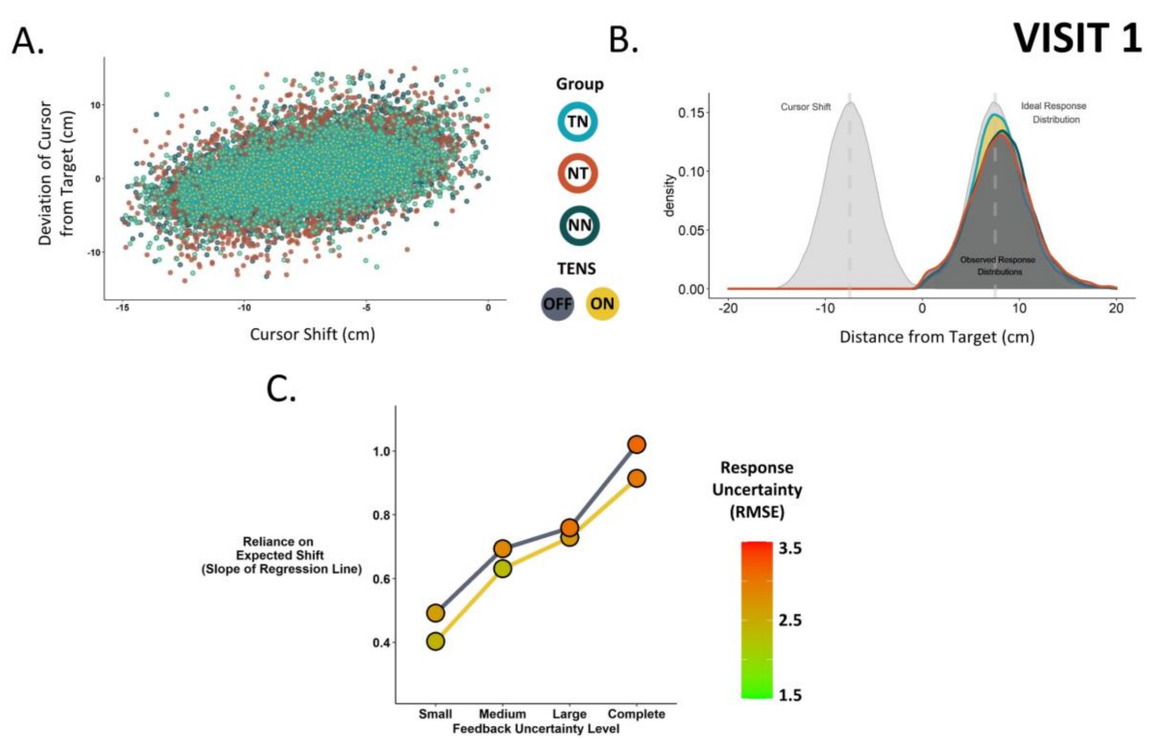


Figure 4.7. Trial analysis for visit 1. A. Scatter plot of all trials on visit 1 sorted by group and TENS condition. B. Response distributions of all groups' responses compared to the cursor shift distribution and ideal response distribution. C. Reliance on expected shift and response uncertainty for group NT (gray) and group TN (yellow).

of the cursor shift and the ideal response distribution. Group TN's responses are a better fit to the ideal response distribution compared to group NN and group NT who are very similar to one another and both did not receive TENS on their first visit. Figure 4.7 C demonstrates the differences in reliance on the shift and response uncertainty between group NT and group TN on their first visit. Group TN, who received TENS, relied less on the expected shift and more on their sensory input in all feedback uncertainty conditions when compared to Group NN, who received no TENS. Furthermore, the response uncertainty for group TN was also less than group NT in all feedback uncertainty conditions. On the whole, the group that received TENS stimulation in visit 1 relied less on the expected shift and showed less uncertainty in their responses when compared to the other groups.

Visit 2

Figure 4.8 shows the results from all trials in visit 2. Figure 4.8 A shows a scatterplot of all trials from all participants identified by color. Figure 4.8 B shows the response distributions for all three groups on visit two compared to the distributions of the cursor shift and the ideal response distribution. Group TN's responses are a very similar fit to the ideal response distribution whereas the distributions of group NN and group NT are very similar to one another. Figure 4.8 C demonstrates the differences in reliance on the shift and response uncertainty between group NT and group TN on their second visit. Group TN, who received TENS on their first visit but not their second, relied less on the expected shift and more on their sensory input in all feedback uncertainty conditions when compared to Group NN, who received TENS. Moreover, the response uncertainty for group TN was also less than group NT in all feedback uncertainty conditions. Overall,

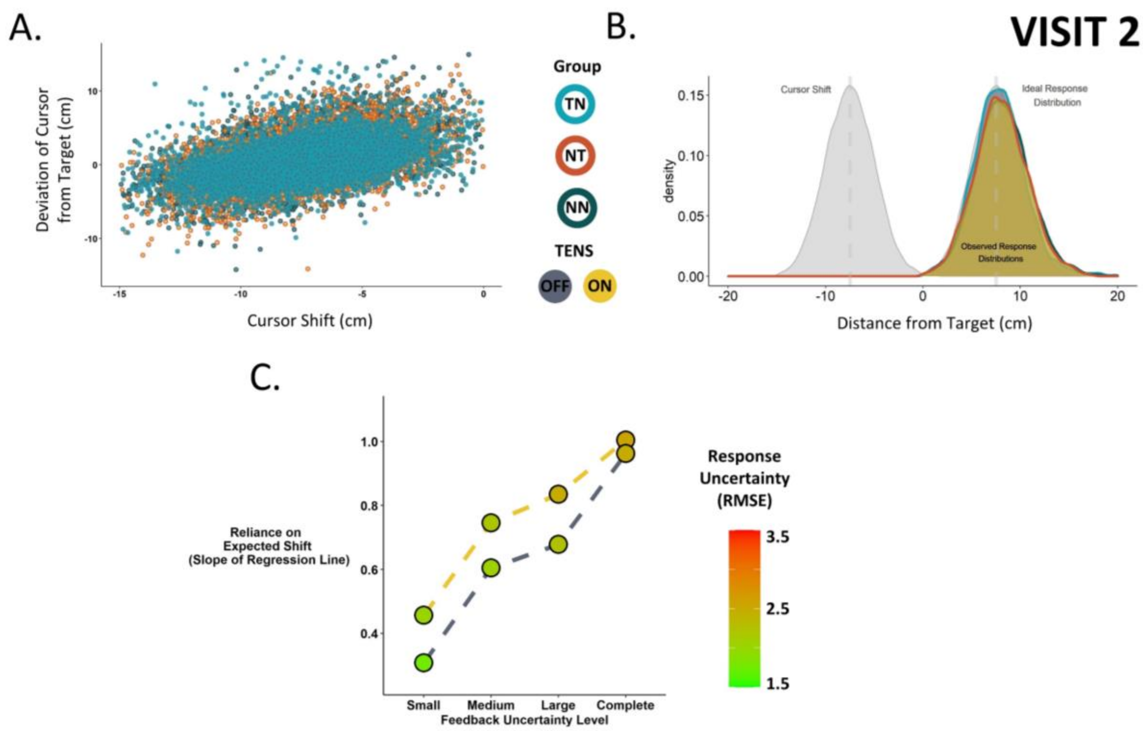


Figure 4.8. Trial analysis for visit 2. A. Scatter plot of all trials on visit 2 sorted by group and TENS condition. B. Response distributions of all groups' responses compared to the cursor shift distribution and ideal response distribution. C. Reliance on expected shift and response uncertainty for group NT (yellow) and group TN (gray).

group TN relied less on the learned expectation of body position when receiving TENS in the first visit and displayed less uncertainty in their responses when compared to group NT who did not receive TENS, and this difference between groups was consistent in their second visit when group TN did not receive TENS and group NT did receive TENS.

Discussion

The purpose of this study was to clarify the underlying mechanisms that lead to the observed improvements in gait and balance that are seen with the use of TENS. To address this purpose, I applied a theoretical model of Bayesian inference to measure and assess sensory uncertainty and how it influences body position estimates during a full body stepping movement. Furthermore, I applied a crossover study design that consisted of three study groups performing the Bayesian motor learning assessment on two separate visits either with or without the addition of concurrent TENS. All methods of these analyses corroborate the hypothesis that TENS decreases the uncertainty that participants showed as they were required to estimate body position in the assessment. The following pages will elaborate on how the measurements of sensory reliance and uncertainty were deduced from the Bayesian motor learning assessment as well as address the main findings gathered from this study.

As I performed the analysis of all groups, both at the participant level and at the trial level, I observed that the response uncertainty variable decreased with the addition of TENS. However, the response uncertainty metric that was used in this study is a latent variable that cannot be directly observed but rather, was taken from the RMSE of the regression line between the cursor shift on each trial and the observed cursor accuracy on the same trial. This approach towards assessing the uncertainty within a participant is based off the methods of (Kording & Wolpert, 2004a) and feed off the overall theory of Bayesian statistics. Bayesian statistics are used to decrease the uncertainty when estimating an unknown parameter and the available evidence is clouded with uncertainty. In this way, the uncertain available data is combined with previously collected data (accompanied by its own variability) to calculate a probability distribution that provides the optimal estimate for the unknown parameter with the least degree of uncertainty. In the context of Bayesian inference in motor control, the available evidence is the sensory data acquired by various sensory receptors and relayed to the CNS to provide essential updates on bodily states and environmental variables.

Sensory data of all types is clouded with noise and uncertainty and, as a result, leads to variability in the perceived body state by the CNS (Faisal et al., 2008). However, as we gain experience performing similar types of movements, the CNS is able to store and combine the resultant sensory data of previous motor performances to calculate expectations for both how a movement will be performed, and the sensory data that will result from it (Berniker, Voss, & Kording, 2010; Kording & Wolpert, 2004b; Shadmehr et al., 2010; Wolpert & Ghahramani, 2000). According to Bayesian inference in motor control, the ideal estimate for the state of the body comes by combining the two sources of information in a Bayes optimal way to maximize the accuracy and minimize the uncertainty in the final position estimate (Berniker & Kording; Kording & Wolpert, 2006; Körding & Wolpert, 2004). In this study, I control the uncertainty of expected body positions by first teaching participants to expect a backwards shift to the cursor they see that is controlled by their CoM. The distribution of this shift is meant to represent the distribution of the learned expectation, or the prior distribution as referred to in Bayesian statistics.

I manipulated the uncertainty of available sensory information in two ways: First, I influenced the level of visual feedback uncertainty by adding noise to the location of the cursor controlled by their CoM. In the medium and large feedback conditions I added two-dimensional Gaussian noise to the cursors location with a mean equal to zero and a standard deviation of 2.5 and 5 centimeters, respectively. This is one way that I manipulated the uncertainty of incoming information, or the likelihood distribution referred to in Bayesian statistics. The second way that I manipulated sensory information is with the addition of TENS. The CNS incorporates all sensory information to calculate an overall body position estimate, though many variables dictate how much influence a singular sensory source has on the final estimate (Peterka, 2018). Accordingly, the addition of TENS while performing the Bayesian motor learning assessment certainly influenced the uncertainty in incoming sensory information, whether for good or for bad. It was my hypothesis that TENS would decrease the uncertainty of incoming sensory information which would be made evident as participants decided the position of their CoM in the assessment.

Participants' responses on each trial display how they combined the available sensory data (systematically manipulated as we've previously discussed) with the learned expectation for their CoM position (obtained during the training block as they learn the backwards cursor shift). The characteristics of participants' responses allow us to infer how they combined these two sources of information. In Bayesian inference, the optimal combination of the prior and likelihood distributions is known as the posterior distribution and is influenced most by the source with the least variability. If the likelihood has less variability than the prior distribution, the mean of the posterior will be more influenced by the likelihood distribution. In addition, the posterior will display less variability than in circumstances where the likelihood is more variable. In the context of this experiment, the cursor shift constantly varied and was drawn from a continuous variable (N~(μ = -7.5, σ = 2.4), so the magnitude of the cursor shift was never duplicated and no two trials shared the same shift. As a result, I don't have a distribution of responses for each cursor shift amount that can be observed to infer how participants combine both sources of information. Rather, we can observe the linear relationship between the cursor shift and how it influenced participants' responses across all conditions of feedback uncertainty.

As mentioned previously, the slope of the linear relationship informs us of the influence that the expected cursor shift (the prior distribution) has on position estimates. However, I use the RMSE of the regression line to infer the variability of the posterior distribution, i.e. participants' resultant estimate of body position based on the available sensory data and the learned expectation of body position. The RMSE is a measure of how concentrated the observed data is around the line of best fit. In the context of this study, I am using it to represent the posterior distribution and the variability that accompanies it. A higher RMSE represents a higher degree of uncertainty in participants' responses. Figure 4.9 displays the data from two participants on the first visit of their participation. Participant #53 received TENS while performing their trials whereas participant #67 did not. As can be observed from their respective data, the participant who received TENS

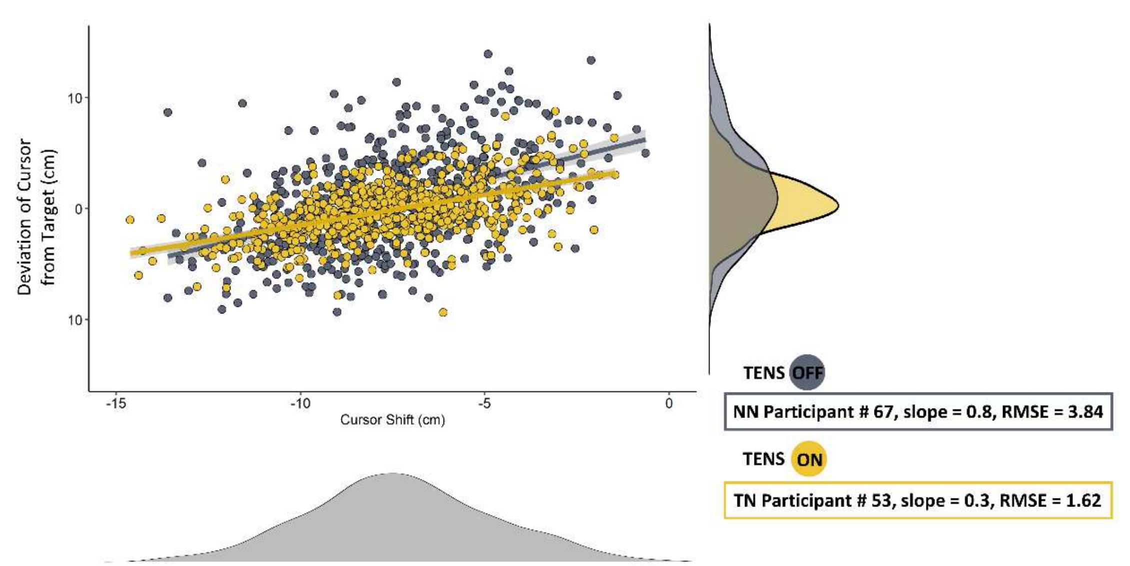


Figure 4.9. Scatter and density plots of NN participant # 67 (gray) who received no TENS and TN participant #53 (yellow) who received TENS. These data are both from visit 1 in the small feedback uncertainty condition. Differences between participants in the relationship between the cursor shift and the deviation of the cursor from the target are evident in the slope of the regression line and tightness of the fit suggesting that participant #53 relied more on incoming sensory input and less on the expected shift and showed less uncertainty in their responses.

displayed a tighter fit to their regression line than the participant who did not. In this small comparison, and when considering all participants, I found that the addition of TENS reduced the uncertainty in participants' responses.

The exact mechanisms that lead to the decrease in positional uncertainty due to TENS remain to be seen. Previous work using various methods of peripheral stimulation of sensory fibers have suggested stochastic resonance may be a large reason for the benefits that accompany these types of sensory augmentation (Ross, 2007; Zéronian et al., 2021). In this sense, the electrical stimulation provided by TENS may add low-level noise that enhances the detection and transmission of weak sensory signals by amplifying the total signal and, as a result, the sensory cues most important to coordinating the current motor task. Furthermore, Paillard (2021) suggests that this also can change the ion permeability of the mechanoreceptors (group Ia and IIa afferents of muscle spindles) priming them, in a sense, to make them more likely to fire action potentials and increase sensory input to the brain and spinal cord. Applying a similar study purpose to decrease sensory uncertainty, Macerello and colleagues (2018) applied peripheral nerve stimulation with high-frequency vibration to the muscle of the wrist as healthy and clinical participants completed a battery of upper extremity motor tasks. They found that both groups decreased completion time of the motor tasks and showed a decrease in EEG beta power over the sensorimotor cortices as they received the stimulation. Altogether, these results combined with previous research, support the hypothesis that TENS, and other methods of afferent stimulation, improve motor performance by decreasing the noise inherent to sensory data and permitting users to be more certain of their body position as they perform motor tasks.

Furthermore, I showed that group TN, who received TENS on their first visit only, demonstrated the least reponse uncertainty in their first visit when compared to other groups on the same visit. Interestingly, group TN went on to further decrease their response uncertainty in the second visit where they didn't receive TENS and still reported less uncertainty than both groups on the second visit. A constant concern that is associated with many forms of sensory augmentation is whether or not any observed benefits will persist once the additional sensory stimulus is removed. One implication of these findings is that, at least in certain circumstances, the benefit that is gained from the addition of TENS while learning and performing a new movement is retained in future performances of the same movement. Furthermore, when compared to group NT who received TENS in their second visit, it seems that TENS is most beneficial when it is applied early in the motor learning process. Recent work has shown that when learning a new motor skill, functional changes occur in the somatosensory cortex to process incoming sensory data prior to any observed changes in the specific motor areas of the brain (Mirdamadi & Block, 2020; Ohashi et al., 2019). Taken together, this further emphasizes the importance of sensory input to motor performance and specifically to motor learning. As mentioned previously, Bayesian motor control theory posits that the CNS combines incoming sensory information with learned expectations of body position based on previous attempts. However, when performing a novel movement, expectations of body position are often ill-informed or absent altogether. In this case, learning the physical and sensory consequences of a new motor skill is a priority to ensure accurate position estimation and movement performance. From this perspective, it seems logical that enhancing the incoming sensory information with TENS would assist the CNS in identifying pertinent sensory information that informs it of bodily states while performing new movements. The finding that this benefit is retained and even continues to improve following a two-week washout period is compelling and merits the need for further examination. An intervention as simple and cost-effective as TENS could be incredibly beneficial to clinical populations striving to learn, or re-learn, new motor skills in response to injury or disease.

I implemented two different methods of analyzing the data in this study. The first way involved reducing all of participants' six hundred trials down to eight values. This method has been utilized in previous research (Kording & Wolpert, 2004a; Vilares & Kording, 2017) as well as in previous chapters of this dissertation. I found no significant differences in the slope variable, which is used to measure the degree of reliance on the learned expectation, between groups or visits. This lack of findings may be due to a need for more trials for each participant. Indeed, previous work using similar methods has involved test sessions with more than one thousand trials per visit for each participant (Kording & Wolpert, 2004a; Vilares & Kording, 2017), while I only include six hundred trials per study visit in this study. The amount of trials included per session of this study was specifically determined based off the increase in energetic demands that accompany a full-body stepping motion when compared to the simple upper extremity tasks used in previous work. While this reduction in trials may be seen as a limitation, I believe that it is necessary for the nature of the task and will be especially pertinent if these methods are to be utilized in clinical populations, such as MS, where increased levels of fatigue greatly influence the appropriate physical exertion involved in a research study. To address this concern, I performed an additional level of analysis combining all trials performed in the study by all participants. Using this method, I saw differences in the slope variable that wen unnoticed in the participant level of analysis.

I found that the addition of TENS enhanced participants' reliance on incoming sensory information and led to them relying on the learned body expectation less. In this research project, I have shown that the Bayesian model of motor control is effective at identifying improvements in sensorimotor uncertainty. If these methods are to be used in future attempts to research sensorimotor uncertainty in clinical populations, I believe the trial level of analysis may be most beneficial to accommodate for limits on the amount of trials participants may be able to perform.

Interestingly, I found that the addition of TENS had no effect on static balance, as assessed by the mCTSIB. Also, I observed that there was no difference in balance performance between each study visit. The consistency of findings in the mCTSIB validates previous work showing there to be no learning effect of the mCTSIB assessment (Antoniadou et al., 2020). However, the lack of effect of the TENS is contrary to the third hypothesis. Much previous research has found external electric stimulation of the lower limbs to be effective at improving balance metrics (Magalhães & Kohn, 2014; Woo et al., 2017; Zéronian et al., 2021). However, Paillard et al. (Paillard, 2021) recently found that participants' responsiveness to electrical stimulation of sensory nerves to improve balance depends on their baseline balance abilities. This study included only young participants that historically have exceptional balance abilities. It is possible that any effect of TENS on balance performance in this healthy population goes unnoticed because they are already proficient at controlling balance. Also, it is of interest that much of the previous research that has shown improvements in performance with the addition of TENS included methods of assessment that were much more dynamic in nature requiring movement of many joints in multiple planes of motion in contrast to the static conditions inherent to the mCTSIB balance assessment (Almuklass et al., 2020; Kwong et al., 2018).

In conclusion, I demonstrated that TENS applied to the muscles of the lower extremities while performing a multi-directional full body stepping motion decreases the uncertainty in sensory information and improves participants' estimation of the location of their CoM. Furthermore, I demonstrated that the Bayesian model of sensoimotor uncertainty can be used to assess and measure the underlying processes that benefit from a therapeutic device aimed at improving sensory function. Future work applying these findings and methods to various contexts is needed to further understand the underlying mechanisms that enable effective gait and mobility in all populations.

CHAPTER 5 – CONCLUSION

Movement is the result of efferent electric signals sent from the CNS that cause the contraction of muscles in the periphery. This movement causes a dataset of sensory information to be sent back to the CNS that is used to determine the efficacy of the previous motor command. Because it is the motor signal that ultimately causes movement, attention aimed at improving the neural control of movement has focused on the motor aspect of movement control. For example, rehabilitation practices to maintain/improve mobility in clinical populations are dominated by resistance and endurance training (Cadore et al., 2013; Gunn, Markevics, Haas, Marsden, & Freeman, 2015b; Mak et al., 2017; Pogrebnoy & Dennett, 2020). Training for athletic performance centers largely around speed and strength training (Lloyd et al., 2016a). It is not the intent of this dissertation to suggest that those practices are ineffective or overutilized. Rather, I advocate the development and use of rehabilitative/training practices that enhance the sensory aspect of human movement in addition to the previously accepted "gold standard" methods of improving movement. Part of the reason that proprioceptive training has previously been neglected is due to its difficulty to measure in a way that is consistent with the goal-directed movements of our daily lives (Han et al., 2016b; Krewer, Van de Winckel, Elangovan, Aman, & Konczak, 2016). Recent developments in VR make it a prime contender as a method to address this inherent difficulty. I believe that as methods to assess proprioception improve, so will the general understanding of its role in effective movement.

This dissertation provided evidence to emphasize the substantive role of sensory information in this process. An individual with a higher functioning sensory system can perceive body states that more accurately resemble their true state. As a result, their ability to construct a movement plan will benefit movement performance. Thus, a person's movement is only as good as their ability to sense themselves performing it. Conventionally, training protocols aimed at improving motor function rely on multiple repetitions to provide the individual multiple opportunities to perform the correct motor commands. The evidence stated in the previous chapters suggest that it may be beneficial to approach training protocols with the perspective of giving individuals multiple opportunities to feel the sensory consequences of correct motor commands. Flanagan et al. showed that once an individual is able to predict the sensory consequences of a movement, the appropriate neural changes occur to consistently and accurately control the motor system to perform the movement (Flanagan et al., 2003). Along those lines, Adams and colleagues suggest that it is the sensory prediction that actually descends the spinal cord and the resulting motor command occurs via reflexive mechanisms (Adams, Shipp, & Friston, 2013). Further work need be done to clarify this suggestion but nevertheless, it emphasizes that the sensory information resulting from motor commands is a fundamental component of movement control. This is made evident when considering the priority placed on acquiring and transporting somatosensory information as well as vital neural processes employed to effectively use sensory information to control movement.

Summary

The three research studies included in this dissertation examined how the central nervous system (CNS) estimates center of mass (CoM) position while performing a full body dynamic mobility movement. In all three studies, this was examined by applying the statistical model of probability Bayesian inference as a model to understand how the CNS addresses uncertainty in sensory information. Previous work applying Bayesian inference in a similar way has examined only simple upper extremity movements. To facilitate the application of this model to a dynamic full body movement, I built a virtual reality (VR) program that mimicked the task constraints used in previous Bayesian work but allowed for the necessary movements in the full body task. Using this VR program I then investigated the Bayesian model of position estimation as it applies to the full body stepping task instead of a simple arm task, as has been seen previously. I also investigated how sensorimotor uncertainty impacts body position awareness for individuals with varying levels of sensorimotor competence with the purpose of better understanding how the Bayesian model can be applied to all manners of populations. In my last study, I used the Bayesian model to better understand the impact that transcutaneous electric nerve stimulation (TENS) has on balance and mobility.

This research is beneficial because there is a great need for specific approaches to assess sensory function in all population. Much recent work has suggested that somatosensory information plays a much larger role in movement than has previously been understood and I believe it is an area of scientific intervention that has been underdeveloped as a way to improve skilled motor performance in all populations. Due to this increased appreciation for somatosensation's role in motor performance, there will continue to be a surge of interest in understanding the crucial neural processes involved. With this increased interest need also come an appreciation for the complex nature of somatosensation and how it informs motor control. The findings form these three research studies provides important insight into how the CNS uses sensory information during movement and into how we can better assess sensorimotor function.

In the first study, I showed that uncertainty in sensory information is taken into account when the CNS estimates CoM position and that learned expectations for CoM position inform this estimation as sensory input becomes less reliable. The second study confirmed that CoM position estimates that better fit the Bayesian model of CoM state estimation are consistently seen in individuals that display superior sensorimotor function. Furthermore, I also showed that individuals with greater sensorimotor function displayed less uncertainty in their own estimates indicating that their somatosensory input was more reliable as they performed the stepping task. These findings demonstrate that we can use the Bayesian model to assess a person's somatosensory function to assess how much it is informing their movement decisions. In the third study I showed that the observed benefits that come from wearing TENS on the muscles of the lower extremities are likely due to the electrical stimulation improving the quality of the somatosensory input coming from the muscles and skin of the involved limbs. These findings are of great importance as we search for simple ways to improve somatosensory function and how to assess them.

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