Mechanisms of Sensory Integration During Postural Adaptation

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DEDICATION

I would like to dedicate this dissertation to my parents for giving me the tools and support necessary to pursue academia and to my wife for her unrelenting support throughout our time together.

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ABSTRACT

The body schema is an internal representation of the position of one's body in relationship to the environment. Adaptation of the body schema involves an update of this internal model in response to changes in the task or the environment. Plasticity of the body schema during postural control allows for one to adapt to changes or hazards in their environment. The level of plasticity is related to the efficiency of integration of sensory feedback in the cortex. This investigation sought to improve the understanding of postural adaptation by identifying the impact of sensory reweighting during a postural adaptation task. Additionally, this investigation sought to identify the effects of bilateral neuromodulation of the posterior parietal cortex (PPC) using transcranial direct current stimulation (tDCS) on postural adaptation. We proposed three experiments to accomplish these goals. During the first experiment, we presented tendon vibration during an incline-intervention, which results an adaptation consisting of an anterior shift in position known as lean after-effect (LAE). During the second experiment, we presented tendon vibration after an incline-intervention. During the third experiment, we performed tDCS prior to an incline-intervention. Primary analyses of the data collected during this investigation revealed that an inclined support surface altered subjects' response to vibration. We also found that vibration during an inclined stance did not alter the development of LAE, but vibration during the after-effect period had direction specific effects. Last, we found that neuromodulation of the PPC led to alterations in LAE. Results of this dissertation

identified effects of proprioceptive reliability on the development of postural adaptation induced by an incline-intervention. Furthermore, this dissertation identified the direction specific results of altered support surface inclination on the effects of tendon vibration, providing new insights to this line of research. Results also help to improve the understanding of the role of the PPC in postural adaptation associated with adaptation of the body schema. These insights may lead to improvements in understanding of the role of the body schema in postural control, which may lead to improvements in strategies for the maintenance and rehabilitation of postural control in aging and disabled populations.

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Introduction

Significance

Falls are among the leading causes of accidental death and injury in the United States. Among people 65 years of age or older, falling is the leading cause of unintentional death [1]. The age group of 85 or greater is the fastest growing age group in the USA, and falling is especially common and hazardous in this group [1]. Roughly 3.2 million falls occur each year in the United States which require medical care [2]. Because that figure is only for falls which require medical care, it's likely that there are more falls which are not severe enough to require a hospital visit. Between 2000 and 2008, it was reported that 18,640 people died annually from falls [3]. More recently, that number has risen to 24,190, suggesting that with an aging population, fall incidence is increasing [2].

Falling rarely results in death, but can often result in debilitating physical, neurological and/or psychological effects. Broken bones are commonly the result of falling. Bones in the arms, shoulders and hips are especially vulnerable, especially in the frail [4]. Traumatic brain injury (TBI) deaths and hospitalizations are overrepresented in older individuals as well [5]. In Americans 75 or older, one in fifty experiences a TBI related hospitalization, emergency room visit, or death. While these data incorporate all causes including motor vehicle accidents, a majority of TBIs are from falls [5]. One third of people 65 or older who are hospitalized after a fall will never be discharged to their home [6]. Not only does this lead to decreases in quality of life and independence, but also high monetary costs. In 2016, fatal falls lead to a monetary burden of $637.5 million per year, while non-fatal falls lead to a cost of over $31 billion per year, which is a billion more dollars than reported in 2012 [2]

Healthy aging, as well as disabilities of the musculoskeletal or neuromuscular system can lead to increased fall risk and fall severity. The likelihood of falling is known to increase with age, but the severity of consequences from falling also increases with age[7]. Physical ailments including muscular weakness, sarcopenia, arthritis and diabetes have all been shown to correlate with increased fall risk [8]. Neurological conditions including cognitive impairments, depression, Alzheimer's, stroke, and Parkinson's disease also increase fall risk [8,9]. People with multiple disabilities, especially those who require multiple medications are at even greater risk for falls [10].

Many neuromuscular and musculoskeletal factors compromise balance performance. One especially important factor is the quality of sensory stimuli and the perception of our environment. Previous investigations have shown that degradation of primary sensory systems (e.g. the vestibular, visual, and somatosensory systems) have an important role in falling [11]. Deterioration of the vestibular system through vestibulopathy or lesion leads to decreased postural stability, especially when visual feedback is unavailable [12]. Many visual conditions contribute to postural instability [13]. Additionally, aging leads to somatosensory loss, leading to greater reliance on visual feedback [14].

Perhaps even more important than the primary sensory feedback is the central nervous system's ability to integrate information from multiple senses into one coherent perception of the environment. Increased integration latency is related to increased fall risk [15]. Aging leads to a decreased ability to quickly and effectively integrate changing multisensory information [16]. The significance of sensorimotor control research is clear based on the prevalence of falls and postural instability in the population. Further postural control investigation will lead to better understanding of the biomechanical and neural mechanisms that we utilize in postural control and will aid in the identification and rehabilitation of dysfunctional factors which lead to falls as well as the aforementioned monetary and human costs related to falls.

This investigation added to the body of understanding addressing postural adaptation and the role of sensory integration in postural adaptation. In order to achieve this, we performed three experiments. For Experiment One, tendon vibration was applied during an incline-intervention in order to identify the effects of tendon vibration on the formation of lean after-effect (LAE). For Experiment Two, tendon vibration was applied following an incline-intervention in order to identify the effects of tendon vibration on the extinguishment of LAE. Results from these experiments clarified the outcomes of two concurrent proprioceptive manipulations on postural adaptation. Experiment Three utilized transcranial direct current stimulation of the posterior parietal cortex to probe postural adaptation following an incline-intervention. The results of this experiment helped clarify the role of multisensory integration on posture role of the PPC in sensory integration performance.

Postural Control

Maintaining upright stance during normal posture or gait is relatively easy for a majority of people. This is the case despite the fact that the human body is inherently unstable [17,18]. Humans have a relatively high center of mass (COM), roughly at the height of the navel. The features of bipedal COM, accompanied with only two relatively small support points (i.e. the feet), lead to an unstable body [19]. This instability leads to constant requirement of corrective movements and torques in order to stay upright [17,18].

Postural control is mostly maintained through the use of sensory feedback, which we rely on to guide corrective movements in order to stay upright [17]. This sensory feedback is provided by the proprioceptive, visual, and vestibular senses and is centrally integrated. Through sensory integration we are able to create a representation of our body parts in relation to each other as well as representation of our body's orientation and movement within the surrounding environment, or our body schema [20,21]. Inputs from the proprioceptive, visual, and vestibular systems are prioritized or "weighted" based on their reliability and relevance for maintaining upright stance [22].

Sensory manipulations which evoke postural adaptation are often employed in order to study sensory integration and dynamic sensory reweighting. Two popular proprioceptive manipulations are tendon vibration and incline-interventions. Tendon vibration is known to decrease proprioceptive reliability, inducing dynamic sensory reweighting (i.e. downweighting of the proprioceptive system) in favor of visual and vestibular signals in order to maintain postural stability [23]. Tendon vibration also induces a shift in position towards the vibrated tendon [24]. Furthermore, tendon vibration has been observed to lead to after-effects once vibration is terminated. Wierzbicka et al. demonstrated that shank tendon vibration led to postural adaptation, and an after-effect in the opposite direction after the termination of vibration stimulus [25].

Another method to induce postural adaptation are incline-interventions. During these experiments, researchers systematically alter the inclination of the support surface in order to change the relationship between gravitational upright and upright with respect to the support surface. Previous literature has dubbed this phenomenon lean after-effect or LAE [26]. An incline-intervention (i.e. positive inclination) is followed by a forward shift when the individual returns to standing on a flat surface in the absence of vision. The LAE phenomenon is an example of plasticity of the body schema and postural adaptation [27–29]. The adaptation takes minutes to decay [30,31]. Responses to an incline-intervention depend on the relative sensory weight one places on each sensory system. People with dominant vestibular systems will prioritize vestibular inputs when vision is unavailable, while somatosensory dominant individuals will prioritize somatosensory and proprioceptive information when vision is unavailable [32]. Previous research has shown that somatosensory dominant individuals exhibit LAE while vestibular dominant individuals do not [30,31].

The Posterior Parietal Cortex

Recent investigations have suggested that the Posterior Parietal Cortex (PPC) is highly involved in representation of postural preferences in the brain of rats [33]. This is augmented by anatomical studies showing that the PPC has reciprocal innervations with almost all sensory areas of the brain [33,34]. These investigations have been extended to show multisensory integration and extra-personal space representation occurs in the PPC of monkeys [35]. Similarly, human studies have shown that the PPC is involved in aspects of multisensory integration and involved in resolving feedback disputes [36–38]. Together, this information suggests that the posterior parietal cortex is intimately involved in creation of the body schema[39,40]. Furthermore, neuromodulation of the PPC has been found to alter integrative capabilities as well as motor adaptation[39,41,42]. Transcranial direct current stimulation (tDCS) is an increasingly popular tool to study motor control, and essentially involves the injection of small amounts of electrical current into the brain through small saline soaked sponges. The charge flows through brain tissue from electrodes. Flowing from anode(s) to cathode(s). The area under the anode receives a small positive electrical stimulation, which leads to relative depolarization of the neurons in the area making action potentials more likely to occur. The area under the cathode receives the inverse, a small negative electrical stimulation, which leads to a relative hyperpolarization of the neurons in the area making action potentials less likely to occur. Electroencephalography and TMS studies have shown that tDCS can modulate resting membrane potential, beyond the alteration of cerebral blood flow described by Zheng et al. [43,44].

Recently, both Mimica and Chen, using animal models, have concluded that the PPC houses specific postural control neurons which integrate sensory information specifically for the task of postural control [33,34]. Holmes and Spence (2004) argued that the PPC was intimately involved in multisensory representations of peripersonal space, body schema[29,40]. Studies have demonstrated that neuromodulation of the PPC leads to alteration of sensory integration capabilities [41,45]. Bruno et al. recently reported that tDCS of the PPC alters the perception of motor illusions. In their experiment, Bruno et al. performed anodal or cathodal tDCS over the premotor cortex or the PPC finding that stimulation of the premotor cortex did not alter perception of hand twitches but stimulation of the PPC did [46]. Additionally, studies have found that sensory integration is impaired in PPC stroke [47]. Given the role of the PPC in postural perception and body schema, these findings should not be a surprise [33,34,40,48].

Motivation

Major health issues face society as the population continues to age. Heart disease, cancer, metabolic disorders and neurodegenerative diseases are all commonly known to prematurely decrease quality of life and lead to many preventable, early deaths. Impairments in motor control, be them from specific disabilities such as Parkinson's Disease or Stroke, or a product of typical aging, also have a large impact on health. In older individuals, falling is the leading cause of unintentional death [1]. The silent generation, those aged 85 or more, is the fastest growing population group in the United States and is especially vulnerable to falls [1].

Scientists do not fully understand the neuromuscular and musculoskeletal factors which comprise postural control. Sensorimotor control, or how one uses sensory feedback to inform movements, is an important factor in balance. Previous investigations have shown that degradation of primary sensory systems (e.g. the vestibular, visual, and somatosensory systems) have an important role in falling [11].

Sensory integration, the central nervous system's ability to combine information from multiple senses into a single perception of the environment, or body schema, is an important line of research to address postural dysfunction. Aging leads to a decrease in the efficiency of sensory integration [16]. The significance of sensorimotor control research is clear based on the prevalence of falls and postural instability in the population. Further postural control investigation will lead to better understanding of the biomechanical and neural mechanisms that we utilize in postural control and will aid in the identification and rehabilitation of dysfunctional factors which lead to falls as well as the aforementioned monetary and human costs related to falls.

To date, mysteries remain in the world of sensorimotor control and sensory integration. We do not fully understand the phenomenon of postural adaptation as it relates to changes in sensory reweighting. We also do not fully understand the brain regions related to postural adaptation. By using three different interventions: incline-interventions [31], tendon vibration [24], and transcranial direct current stimulation of the posterior parietal cortex [49], it may be possible to improve our understanding of this phenomena which could in turn aid in quality of life in aging and disabled populations.

Problem Statement

Previous studies have identified lean after-effect as a type of postural adaptation. These studies have suggested that both the reliability of proprioceptive information, and multisensory integration capabilities, are related to the magnitude of lean after-effect. As of yet, studies have only utilized methodologies which only induce alterations in weighting of sensory feedback (i.e. augmented feedback through light touch, systematic elimination of visual feedback, or inhibited reliability through sway referencing). To date, no investigation has identified the effects of a concurrent intervention which not only alters proprioceptive reliability but also induces adaptation of body position.

Furthermore, there is a relative lack of understanding of the cortical mechanisms which influence adaptation of the body schema. While previous investigations have identified cortical areas relevant in the creation of the body schema (i.e. the ventral premotor cortex and posterior parietal cortex) and identified cortical regions which are relevant in postural control (i.e. the primary motor cortex and cerebellum), little investigation has sought to identify the role of the posterior parietal cortex in adaptation of the body schema in the realm of postural adaptation.

Experiments to further elucidate the processes of postural adaptation are going to be crucial in furthering the understanding of postural control and informing applied studies and health practitioners on practices to improve postural adaptability. The current gaps in understanding the processes of postural adaptation led to this investigation's questions:

Research Questions

Question 1: Does tendon vibration during an incline-intervention alter lean after-effect?

Question 2: Does tendon vibration following an incline-intervention alter lean after-effect?

Question 3: Does performing tendon vibration during inclined stance or following an incline-intervention alter the direction-specific effects of vibration on COG position?

Question 4: Are there differences in vibration-induced increases in postural sway between differing support surface configurations?

Question 5: Does stimulation of the posterior parietal cortex alter lean after-effect?

Research Objectives

The primary goal of this dissertation was to identify interventions which could alter lean-aftereffect. The outcomes of the experiments serve to improve our understanding of postural adaptation and therefore adaptation of the body schema. To achieve this, we performed three conceptually linked but independent experiments.

Experiment 1. This experiment was designed to answer research Question 1. Comparisons were made between resulting lean after-effect of three conditions of incline-interventions. The three conditions were: no vibration throughout, Achilles tendon vibration during inclined stance, and tibialis anterior vibration *during inclined stance.* In order to compare lean after-effect, Integrated Area and Off-Set Time of significant anterior lean were computed and compared between conditions. In order to identify positional differences between different support surface configurations during vibration, average position of the center of gravity was compared before, during, and after tendon vibration. In order to identify whether inclined stance effected the increase in sway present during vibration, anterior-posterior sway, AP-Path length of the COG, was calculated. These data were compared within a group of 15 healthy, young subjects with no history of neurological or musculoskeletal disabilities that may impair postural control or sensory feedback.

Experiment 2. This experiment was designed to answer research Question 2. Using the same subject group, three conditions of incline-intervention were compared. Integrated Area and Off-Set Time were compared between incline-interventions which were either free of vibration, or included tendon vibration of the Achilles or tibialis anterior tendon *following inclined stance, lean after-effect*. Data from this experiment was also utilized in the comparison of positional and sway-related alterations in the response to vibration based on a previous bout of inclined stance. Together, Experiments 1 and 2 answer research Questions 3 and 4.

Experiment 3. A second group of 15 young, healthy subjects were presented three conditions of transcranial direct current stimulation of the bilateral posterior parietal cortices. Using this population, Experiment Three aimed to answer research Question 5. Subjects underwent randomly and double-blinded bouts bilateral transcranial direct current stimulation which included Sham, right-anodal/left-cathodal (RA-LC) and right-cathodal/left-anodal (RC-LA) conditions. Following stimulation, subjects underwent an incline-intervention. Lean after-effect was compared between conditions.

Hypotheses

Question 1. It was hypothesized that tendon vibration during an *incline-intervention* would inhibit lean after-effect compared to a control incline-intervention.

Question 2. It was hypothesized that tendon vibration *following an incline-intervention* would lead to direction-specific alterations in lean after-effect based on which tendon is vibrated.

Question 3. It was hypothesized there would be no effect of support surface inclination on vibration-induced shifts in position.

Question 4. It was hypothesized there would not be differences between vibration-induced changes in sway during flat, inclined, or post-inclined stance.

Question 5. It was hypothesized that stimulation of the posterior parietal cortex would lead to (current) direction-specific alterations in lean after-effect.

2.0 Literature Review

Sensory Systems

One's ability to move effectively through the complex and ever-changing world that they experience daily requires constant input which allows for an accurate perception of the environment. This information comes from several sensory systems. Peripheral neurons in these sensory systems are activated by environmental stimuli, and once activated they send information through afferent pathways towards the central nervous system (CNS). The CNS then performs uses this data to create a conscious experience of the world, or body schema[29,50]. There are many senses including hearing, smell, and taste, but the senses that are most interesting for human motor control are somatosensation, vision, and equilibrioception, the sense which arises in the vestibular system.

Somatosensation

Somatosensation is an umbrella for the sense of position, and movement. For the purposes of this literature review, the portion of somatosensation that is the most relevant is proprioception. Proprioceptive receptors are excited by position, tension and movement. They relay these signals to the CNS [51]. These signals form the conscious perception of position and movement [52]. Together these perceptions form the body schema, or the sense of one's own body [53]. There are dozens of somatosensory organs, but the primary organs for proprioception are muscle spindles, Golgi tendon organs, and joint receptors. All three of these receptors are utilized to some degree in both body orientation and balance control [54].

Muscle spindles lie parallel to extrafusal muscle fibers and sense changes in length of skeletal muscles. These arise to provide perception of position and movement of the body's limbs [55,56]. This means that muscle spindles contribute to the sense of kinesthesia [57]. Gama motor neurons innervate the muscle spindle and are activated by the muscle spindle's elongation due to deformations of the spindle, and which coincides with the lengthening of the muscle [58,59]. Important information which is used for sensory feedback of posture and movement arises from these sensory organs.

Golgi tendon organs lie in the musculotendinous junction sense changes in tension, providing feedback for movement effort and providing a safety related reflex to inhibit muscle contraction if tension reaches extreme levels [60,61].

Joint receptors are another mechanoreceptor that are embedded in the joint capsule which are mostly active near the limit of a joint's range of motion. They provide information related to joint position and movement [62]. Together muscle spindles, Golgi tendon organs, and joint receptors, among others, make up the proprioceptive system.

The proprioceptive system is used to perceive body orientation, how each segment is positioned relative to each other and to the world [54]. Proprioceptive information is processed in the spinal cord, as well as the brain stem and the cerebellum but also in higher level cortical areas [63]. Pleger et al. reviewed haptic stimulation investigations which used fMRI and found activity in the primary somatosensory cortex, secondary somatosensory cortex, and the superior and inferior parietal lobules (IPL), part of the posterior parietal cortex (PPC) [50]. Haptic sensation does not, however, directly involve movement perception. Using matching tasks to study proprioception, Iandolo et al. found brain activation in the parietal, motor, frontal areas as well as the cerebellum [63]. Furthermore, it has been found that the PPC is a critical brain area in proprioceptive spatial mapping, utilizing proprioceptive information to build a representation of the body's position and movement in space [64]. The above research highlights the diffuse CNS areas which are important in processing proprioceptive information.

Proprioceptive organs are stimulated by simple changes in the body, but the perceptions that arise from proprioception are complex and can be made dysfunctional by a multitude of pathologies. Strokes often lead balance issues. One reason for the balance issues may be due to stroke related somatosensory impairment [65]. The precise systems which are affected depend on the lesion, with stroke in the PPC leading to what was once termed a "pure sensory stroke" [47]. Strokes that do lead to basic impairments of the somatosensory system tend to lead to balance deficits [66]. These deficits are more obvious during gait than static balance tasks [67]. Parkinson's disease is another disability that decreases postural stability. One of the first measurable impairments which occurs in Parkinson's disease is decreased somatosensory function, according to a review by Conte [68]. Evidence of somatosensory deficits in Parkinson's is apparent in the performance improvements which Parkinson's patients have with augmented somatosensory feedback when compared to healthy older adults [69].

While many disabilities lead to decreases in somatosensory function, declines in function can also be observed in the healthy aging. Proprioceptive function decreases with aging [70]. Shaffer and Harrison, in their 2007 review, outlined the various causes of peripheral sensory decline during aging. Starting distally before moving towards the proximal, demyelination of sensory afferents occur during aging. Additionally, over time, morphological changes in the sensory organs themselves lead to impaired function [71]. Moving centrally, there is a modulation of brain activity during proprioception tasks in older individuals. Brodoehl et al. found over-activation of the contralateral primary somatosensory and ipsilateral primary motor cortices in older adults, probably due to insufficient inhibition. The same study found an increased threshold for sensation in order to perceive movement [72]. The degradation of sensory organs and peripheral nerve fibers, as well as altered brain activity leads to decreases in motor control [73,74]. In fact, investigators have suggested that proprioceptive deficits are the most important predictor of falls in the elderly, more than weakness, frailty or any other sensorimotor deficit [75]. Specifically, the morphological issues in sensory organs and demyelination of their afferent nerve fibers leads to impaired distal lower body proprioception (e.g. that of the feet and ankles) before most other issues arise, which leads to poor balance [71]. Decreases in proprioceptive function through peripheral organ or nervous degradation or central perception deficits all lead to diminished postural control capabilities. Proprioceptive dysfunction research is required to fully understand postural control in order to decrease falling in at-risk populations.

Visual System

The second sensory system that is highly involved in motor control is the visual system. Light sensitive rods and cones in the retina of the eyes each attend very specific colors or lights. If the right features are presented, that rod or cone produces an action potential. These action potentials are eventually encoded and processed to provide us a perception of objects and movements around us. There are two primary visual streams, the ventral and dorsal visual streams. Object identification relies on the ventral visual stream while movement perception relies on the dorsal stream [51]. Both of these streams are important for posture and movement control. While the central stream can identify objects in one's environment, the dorsal stream will identify the relationship between the individual and the environment. Vision tends to dominate other sensory modalities in creating our perception of our environment [76]. This explains and is explained by the visual system also being represented by more cortical space for processing than any other sensory system [77]. Vision is important in motor control as we use both the ventral and dorsal streams for understanding our relationship to and movement within the environment [78,79]. Because vision is so complex, postural control may be impaired when conflicts arise and it is difficult to ascertain whether one is moving within the environment, or the environment itself is moving [79].

Object and movement perception is important for postural control, so the many possible causes of visual dysfunction can lead to postural control issues [80]. Visual impairments of many varieties leads to more cautious including gait greater step width and slower walking speed, static balance decreases, and poor performance during foam standing, unilateral stance, and tandem walking [81–83]. Visual impairments are associated with falling include poor visual acuity, contrast sensitivity, depth perception, and decreased visual field [84,85]. Not only do issues that arise from the eyes lead to perception and motor deficits, but lesions in the PPC lead to visuospatial performance issues and lesions in the inferior temporal cortex lead to discrimination task decreases as well [77].

Vestibular System

The third sensory system which has a crucial role in maintaining posture is the vestibular system, which gives rise to the perception of equilibrioception. Mechanoreceptors called hair cells are the underlying sensory organs of the vestibular system [51]. These hair cells are bent by fluid shifting in the surrounding area, which leads to their excitement and the development of afferent action potentials towards the CNS. The utricle and saccule are two vestibular organs that sense head orientation in space and respond to linear acceleration, gravity, and tilting. The semicircular canals together sense rotations in all directions. After a few seconds of static position or constant movement, hair cells return to their normal state and lead us to stop actively perceiving the new position [86]. Tens of thousands of these hair cells send afferent signals to the vestibular ganglion, which leads to the vestibular nerve. Vestibular neurons project to the vestibular nucleus, neurons in the vestibular nucleus have been categorized into two main categories, those responsible for the vestibulo-ocular reflex and those responsible for posture and self-motion, dubbed VO or vestibular-only neurons [87]. Vestibular-only neurons of the vestibular nuclei receive input from the vestibular nerve and then innervate the spinal cord, thalamus and cerebellum as well as parts of the cortex. The VO neurons use information from the vestibular organs to maintain postural equilibrium and send signals for higher-level processing for spatial orientation [87]. While somatosensation and vision perception are both processed in multiple brain regions, each has their own specific, primary brain region. The vestibular system however, projects to a much more diffuse set of brain regions and there is likely no primary vestibular cortex [88]. These diffuse areas include the prefrontal, temporoparietal, contralateral parietal cortices as well as the supplementary motor area and the inferior parietal lobule, which is part of the PPC [88].

Vestibulopathies can lead to intense feelings of motion even when completely still. These issues can lead to severe motor control and postural instability. Vertigo affects 7.4% of people in their life, most commonly in the elderly [89]. The most common form of vertigo is from benign paroxysmal positional vertigo, which occurs when small bones in the vestibular labyrinth move to improper positions. Other common causes of vertigo are the vestibular migraine, vestibular neuritis or peripheral vestibular lesions, and Ménière's Disease. Each of these may lead to dizziness, or a feeling of movement or positioning that is incongruent with visual and proprioceptive feedback, which can be hard to overcome [90,91]. Various vestibular dysfunctions also leads to slower gait than healthy people, as well as a tendency to veer to the stronger side [92]. Vestibular neuritis leads to increased variability during gait especially when visual feedback isn't available, while vestibular migraine decreases stability during quiet stance and coincides with feelings of motion sickness [91,93]. The cause of each of these performance issues may be related to subjective vertical. Healthy people can generally estimate a vertical body orientation fairly well when provided with no other feedback, but vestibular patients have much greater error when reconciling their subjective vertical to actual vertical [94].

The somatosensory, visual, and vestibular systems are all important sources of sensory stimuli which we utilize to perceive the world. Dysfunction of any of these systems may lead to decreased postural control and increased risk of falling. While the signal quality that arises from each system is of importance, the body's ability to create a useful perception through the integration of these multiple sensory systems is perhaps more important [17]. While there is often little possibility to improve some primary sensory dysfunctions, sensory integration can, to some extent, be trained [95]. This means that sensory integration research is vital to understanding the nature of human postural control and improving performance.

Sensory Integration

Perception is a multisensory experience [96]. The signals derived from the somatosensory, visual, and vestibular systems are alone insufficient to provide us with an accurate world-view. Sensory integration in the CNS combines data from all senses to create a perception of the world. Sensory integration allows for the gustatory, olfactory, and visual stimuli from food to be transformed into the perception of a meal as well as an infinite amount of other experiences. For our purposes, however, the three previously reviewed senses and their integration into the perception of posture, movement within, and interaction with the environment are of greater interest. Every sense has unique qualities that provide specific information but naturally does not signal other types of information. Because of this, our perception is much richer after their combination [96]. Integration also helps to make sense of weaker stimuli when they are related to congruent, stronger stimuli [97]. Many factors affect sensory integration including the strength of each sensory stimuli, attention, location, timing, and top-down context based processing [98].

Neurological Basis of Sensory Integration

The neurological basis of sensory integration is understandably complex. Integrating raw signals into a single accurate perception requires processing in several brain regions. Some early sensory integration occurs in the superior colliculus, which has projections to the pre-motor and motor cortices as well as the brain stem and the spinal cord [97]. Another area of interest in sensory integration is the posterior parietal cortex (PPC) as well as its subcomponents (i.e. the superior and inferior parietal lobules). Researchers have found that components of the PPC are active in audio-visual integration, tactile-visual-vestibular integration, and visual-proprioceptive integration [35,96,99–102]. The PPC, including the lateral intraparietal, medial intraparietal, and ventral intraparietal areas, transform sensory signals into a coordinate map for gaze or touch [102]. This leads to involvement of the PPC in all visually guided movements [103]. The PPC has also been shown to be active during both regular gait and backwards walking [104]. Interestingly, the PPC is also innervated by the cerebellum. The cerebellum is responsible for providing an efferent copy of movement error compared to planned motor commands, and the PPC uses this information to better organize coordinate frames [105]. Like all neurological functions, sensory integration extends beyond the superior colliculus and the posterior parietal cortex to involve almost every brain region [102]. Regardless, previous research has shown that neuromodulation solely of the PPC is sufficient to modulate sensory integration and spatial orientation [49].

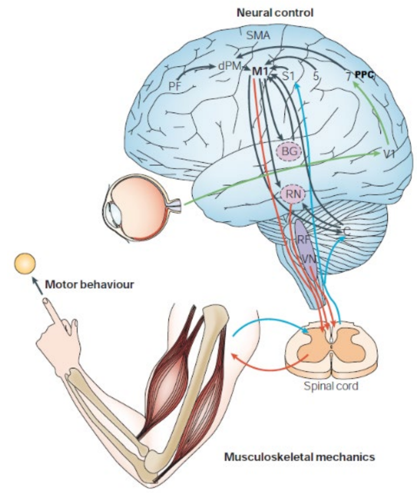

Fig 1. Highlighting brain structures involved in human motor control. From Scott (2004)

For the scope of this literature review, most attention will be placed on sensory integration in postural control. The human body is inherently unstable and acts as an inverted pendulum [17,18]. Humans have a relatively high center of mass (COM) and two relatively small support points (i.e. the feet). This lead to an unstable body [19]. Instability leads to a requirement of constant corrective movements and torques in order to stay upright [17,18]. Even with these difficulties, postural control can be explained by relatively simple feedback models [17]. The requirement for feedback is obvious once we consider the amount of information that would be needed to predict the environment beyond a very short period of time [95]. Feedback from sensory input encompasses most of the information we use to maintain our posture [17]. Some investigations have suggested a need for significant feed-forward control, but others have suggested that feed-forward models may simply fail to account for sensory reweighting [17]. Indeed postural control is based mostly on sensory feedback, and largely influenced by the weights we assign each sensory system, which will be covered more extensively later [106]. It could be said that the combined information of the somatosensory, visual, and vestibular systems is often redundant for postural control. People are capable of maintaining their balance when their eyes are closed, after all. While balance is possible with one sense absent, postural control is decreased [95]. In fact, any change in sensory feedback will have effects on balance [107]. The processing and formation of perception based on sensory feedback is a complicated process. Because there are so many brain regions and computations involved, there are a number of things that can go awry and lead to postural control disabilities.

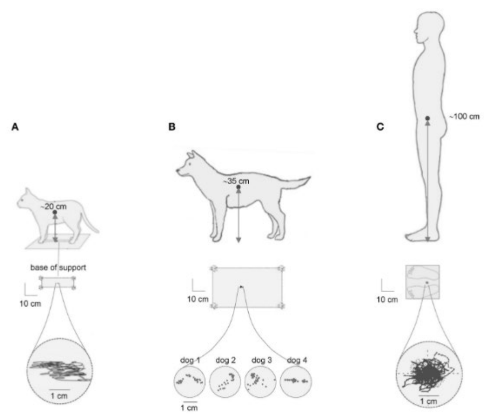

FIGURE 1 | Center of pressure (CoP) fluctuations during quiet standing in the cat **(A)**, dog **(B)** and human **(C)**. Examples of the CoP traces (lower) are adapted from MacPherson and Horak (2012) with permission in **(A)**, redrawn from Brookhart et al. (1965) in **(B)** and modified from Ivanenko et al. (1999) in **(C)**. The size of the base of support is schematically depicted in the middle panels. Note comparable CoP oscillations (~2 cm) in quadrupeds with regard to human despite the 5-fold difference in the height of the center of body mass over the support.

Fig 2. Illustrating the inherent instability of the human postural system. From Ivanenko and Gurfinkel 2018

Just as dysfunctions in sensory systems can lead to postural control deficits, so too can dysfunctions in sensory integration. According to Peterka et al., while diminished sensory function is related to instability, diminished efficacy of sensory integration is more important [18]. Children who are not yet able to effectively integrate sensory information have been the subject of several famous studies. In these investigations, researchers showed young children a moving visual scene that, providing the illusion of movement. Even though they still had accurate somatosensory and vestibular information, the children often fell. This was because despite having fully functioning sensory systems, young children do not yet have fully developed central integration capabilities [108]. Integration deficits are not limited to young children, however. As with primary sensory information, older adults are also more likely to develop sensory integration dysfunctions. For example, even healthy adults are more prone to increased postural sway when presented with visual-somatosensory conflict during quiet stance [109]. This effect is supported by Cohen et al., who sought to identify changes in the Sensory Organization Test (SOT) with aging. The SOT systematically challenges each sensory system in an attempt to identify performance deficits resulting from impairments of each system or integration. Cohen et al. found that SOT scores tend to decrease in age and older people tend to change their strategy towards a somatosensory and visually dominant method of postural control, largely ignoring vestibular information[110]. One could argue that this is merely evidence of greater vestibular loss than somatosensory or visual loss with aging, but other investigations have been performed to isolate sensory integration as the primary reason for age-related decreases in postural control. Teasdale et al., in 1991, demonstrated that when both healthy younger and healthy older adults close their eyes, they experience a period of increased sway. When vision was re-introduced to the young group, sway returned to normal. When vision was re-introduced into the older group however, sway was increased further for a short period [111]. This investigation demonstrated that re-integration of visual information can have a perturbing effect on postural control in older adults, because their integration is not as efficient [111]. This central integration inefficiency leads to greater muscle activation latency, especially with distorted or incongruent sensory feedback [109]. Inefficiency in sensory integration is among the most important reasons for postural instability in older individuals [17].

In addition to healthy aging, several other disorders and disabilities lead to problems with sensory integration. Autism spectrum disorder (ASD) leads to impaired audiovisual integration accuracy [112]. In a training study, Cheldavi et al. identified the effects of sensory integration-focused balance training on postural control in children with ASD [113]. Cheldavi et al. separated primary school-aged children into two groups, one control and one which performed eighteen, 45-minute training sessions comprised of posture and gait tasks which compromised the somatosensory and/or visual systems by the use of a compliant (i.e. foam) surface or closure of the eyes. Comparing pre-and post-intervention postural control in hard and foam surfaces and vision and no-vision conditions showed improved postural control (i.e. less displacement in the AP and ML directions as well as a lower mean COP velocity) in all conditions. These results suggested that balance training involving differing sensory conditions can improve postural control in ASD patients [113].

Fortunately, there does seem to be evidence that the sensory integration deficits associated with healthy aging, as well as the aforementioned and other disabilities, can be partially alleviated through training [114]. In a 2017 publication, Wiesmeier et al., performed ten weeks of balance training in eighteen older adults which included performing static and dynamic tasks while exposed to compliant support surfaces as well as differing visual conditions. After the balance training intervention, older subjects were able to significantly reduce their postural sway. The authors concluded that balance training decreased the older adults' over-reliance on proprioceptive feedback and improved vestibular orientation. This suggests rehabilitation training that specifically challenges sensory integration by providing challenging support surface and visual conditions leads to improved sensory integration performance and postural control [115]. Stroke survivors also have sensory integration deficits, but the severity is highly dependent on the location and size of their lesion [116]. Another method for training sensory integration was employed by Jang and Lee in their 2016 study which aimed to evaluate the efficacy of sensory integration training on improving post-stroke balance. In stroke survivors, lower limb somatosensation is often impaired which leads to increased requirement for sufficient integration and reweighting capabilities in stroke. Jang and Lee used a protocol in which self-and-external destabilizations were performed during standing and walking tasks with and without the eyes closed. The pair found that compared to typical physical therapy, the sensory integration training group improved muscle activation, limits of stability and balance performance to a greater extent, which they believed to be due to improved sensory integration capabilities [117]. Jang and Lee argued that most stroke survivors over-rely on visual feedback, but through training there can be an improvement in reweighting and integration capabilities [117]. Training sensory integration by performing weight-transfer and balance exercises while being exposed to perturbations with and without visual feedback can also improve sensory integration in stroke survivors [118]. Smania et al. aimed to evaluate whether methodically challenging sensory integration performance would be sufficient to improve balance and gait in stroke survivors. Prior to receiving twenty training sessions, patients performed poorly on the more difficult conditions of the Sensory Organization Test (i.e. condition 5 and 6). After training, each such condition improved significantly, which was still evident after a one-week follow-up. Despite the fact that no gait training was performed, there was also a significant improvement in the Ten Meters Walking Test at post-treatment and follow-up times. Because the training consisted primarily on factors designed to challenge sensory integration, Smania et al. believed that the improvement in perturbed balance as well as gait speed can be primarily attributed to changes in sensory strategy. The author concluded that physical therapy which focuses on sensory conflict is ideal in rehabilitating balance and gait for stroke survivors [118]. Bolognini et al. started their recent review by arguing there are no motor-only rehabilitation programs. Even rehabilitation that does not specifically account for sensory training will involve sensory stimulation. Regardless, a stroke rehabilitation approach that specifically accounts for sensory stimulation is likely to have greater success improving motor control [114]. The review continues to argue that stimulating multiple sensory modalities facilitates sensory integration, improving motor responses to changes in the environment. While it is yet unknown the extent in which sensory integration is specifically impaired in stroke there is evidence showing that somatosensory deficits imposed by the brain damage due to stroke can be compensated for by improved sensory integration, as shown by Jang and Lee as well as Smania et al. [117,118]. Eyeing the future, other investigations have also demonstrated that that virtual reality immersion which systematically introduces conflicting sensory data allows for greater ability to efficiently integrate multiple senses after one hour of training [109].

Dynamic Sensory Reweighting

Dynamic sensory reweighting is a critical component of sensory integration in motor control. In their recent review, Saftari and Kwon stated, "Understanding sensory reweighting in older adults may be a stepping stone in understanding falls and in the development of prevention strategies [80]." Our ability to judge the reliability of varying sources of sensory information and integrate that information proportionate to its reliability is critical to successfully implementing corrective balance strategies. According to Nashner (1982), people select the most appropriate, optimal combination of sensory feedback based on the context of their actions and the reliability of the sensory signals [119]. Nashner argued that the CNS was able to identify inappropriate or inaccurate sensory information, and quickly downweight their value and suppress their influence. We perform these judgements about the reliability of sensory cues constantly, and the weights assigned to sensory cues change constantly proportionally to their relative reliability as well [120]. Kabbaligere et al. sought to further the understanding of sensory reweighting with the use of virtual reality visual stimulus combined with tendon vibration. They aimed to identify any interaction between proprioception at the ankle joint and vision when the two sensory channels were provided conflicting information of the direction of body sway. The group used virtual reality goggles to create a visual scene which simulated forward body sway, and used Achilles tendon vibration to induce backwards body sway. Next, they compared sway during three conditions, each of the stimuli being presented individually and the two stimuli being presented simultaneously. The group found that the center of pressure displacement during the combined task was less than the summed displacement during the two stimuli applied individually. Because of this discrepancy, the authors concluded that we do not respond to multiple perturbations in a way that would be consistent with the linear combination of those perturbations (i.e. an anterior stimuli of 2cm and a posterior stimuli of -5cm do not equate to a displacement of -3cm), that reweighting may be an interactive effect combining the reliability-weighted cues in a linear fashion [120]. Temple et al. also investigated sensory reweighting by utilizing shank tendon vibration [121]. The researchers sought to identify the effect of tibialis anterior vibration on center of pressure during support surface translations during quiet stance. Subjects experienced backwards and forward translations with and without tibialis anterior vibration. Center of pressure was compared before, during, and after the perturbation to assess effects of vibration on postural response to a perturbation. The group found that during the recovery phase of a translation, tendon vibration induced a greater anterior shift of the COP. These results, the authors argued, showed that proprioceptive information is continuously reweighted based on the context of the movement [121].

Logan et al. used three conditions in order to study sensory reweighting dynamics during postural control tasks. Subjects were presented with: low amplitude of both visual scene and support surface rotations, high amplitude of visual scene rotation and low amplitude of support surface rotation, and low amplitude of visual scene and high amplitude of support surface rotation. The team measured body sway as well as EMG from postural control muscles. Results indicated that there was intramodality reweighting of vision and proprioception based on the differences in body sway and muscle activity between the high and low amplitude platform rotations but not visual scene rotations [122]. Eikema et al. sought to investigate why older adults require more time to reweight sensory information than younger adults [123]. In order to accomplish this, the group recruited two groups of subjects in order to identify sensory reweighting characteristics in virtual reality environments. Both groups stood atop a force plate performing quiet stance. Subjects were either provided no specific instructions or told to anticipate approaching visual objects that they had to avoid. During each of these conditions, the virtual scene changed every minute from a stationary image of a room to a moving room and then to darkness in order to evoke a change in postural control. The older group exhibited greater sway during transitions of visual scenes during the non-anticipatory condition as well. During anticipation however, the groups did not differ in sway during visual scene transitions. The authors concluded that the anticipation condition interacted with postural anxiety regardless of age, increasing the anxiety of the younger group to match the natural anxiety of the older group. According to the authors, this anxiety, as is naturally present in adults with fear of falling, leads to less efficient sensory reweighting [123].

Assländer and Peterka made a similar finding in 2016 where they periodically altered visual feedback by turning on or off room lights and periodically started sway-referencing the support surface of twelve healthy, young subjects. The group observed changes in sway immediately following transitions in sensory context. The group identified differences in sway responses to different exposures to the same sensory transition. They found that sway responses were somewhat dependent on expectation.

An expectation of an upcoming change in the environment influences sensory reweighting, allowing the individual to select which sensory system is likely to be the most reliable during the upcoming change. These findings were consistent with the earlier study by Eikema et al. [123,124].

Previous modeling has shown a basically linear relationship between reliability and weight, while some small non-linear elements exist in weighting during transition from a more somatosensory dominant to a more vestibular dominant approach to postural control [17]. Ernst and Banks explored this relationship experimentally to investigate the integration of haptic and visual information. They also found a directly proportionate (linear) relationship between reliability and weight when they systematically disrupted visual feedback through prism goggles to increase haptic weight [125]. While Ernst and Banks focused on reweighting based on a single perturbation, Oie and Jeka, in 2002, were able to provide evidence for concurrent re-weighting of visual and somatosensory information [22]. The group performed several posture control task conditions in which the frequency of visual and somatosensory oscillations differed (0.20 and 0.28Hz, respectively). They also manipulated the amplitudes of visual and somatosensory oscillations and the frequency power of center of mass while subjects stood in a tandem stance. The group found that center of mass power changed across conditions and found that the visual and somatosensory gain were dependent on the amplitude of their respective manipulations. Their results, the authors argued, strongly supported the notion that sensory reweighting is a predominant factor in the fusion of multisensory inputs. They found that sensory weights are dynamic variables, dependent on changes in the environment. They also argued for the possibility of simultaneous reweighting of the visual and somatosensory systems.

Previous research by Mahboobin et al has investigated several sensory reweighting paradigms in which one or more systematic perturbations are introduced in order to observe changes in postural strategy and weighting. In one such investigation, subjects were placed in one of two groups. One group was exposed to a static visual scene while the other was exposed to a randomly moving visual scene. After a period of the randomly moving scene, the groups were subjected to postural perturbations. Those who were exposed to the randomly moving scene performed better than those who had not been. The authors suggested that this was due to downweighted visual feedback, leading to upweighted proprioceptive and vestibular feedback aiding them in their ability to respond to the perturbations [126]. Conversely, sway referencing, which entails real-time adjustment of the support surface by shifting forward or backwards as the subject's COP shifts forwards or backwards, a support surface decreases proprioceptive reliability and leads to increased visual weighting [127]. The re-introduction of vision after a period of absence is able to quickly override an erroneous perception based on proprioceptive feedback (i.e. motor illusions). Earhart et al. utilized a lean after-effect (LAE) protocol in order to induce postural adaptation in response to standing on an inclined surface for several minutes. Without visual information, the subject remained leaning forward for several minutes even when they return to a horizontal surface. When vision was re-introduced, however, the subject immediately returned to an upright stance [128]. This suggested a quick identification of unreliable proprioceptive stimuli leading to downweighting of proprioceptive and concurrent upweighting of visual information.

Dynamic sensory reweighting is a component of sensory integration. As such, much if not all of the neurological factors and relevant structures discussed previously are relevant to this topic as well. It has been suggested that there may be two networks specifically involved in sensory reweighting. The perisylvian network, which includes the frontal operculum, right parietal operculum, and superior temporal gyrus may be responsible for the detection of sensory conflict and reweighting based on said conflict. Another network between the posterior parietal cortex and frontal cortex may be responsible to perform sensory integrations based on the reweighted information [129]. Takakura et al. functional used near-infrared spectroscopy (fNIRS) to measure hemodynamics while they employed the SOT on a group of subjects. They identified significant increases in oxyhemoglobin, an indirect measure of brain activity, in several brain regions during challenging SOT conditions. Notably, increases suggested that the frontal areas as well as the posterior parietal cortex are essentially for sensory integration during perturbations of balance. The authors argued that the PPC and pre-motor cortex were involved in updating the spatial reference frames during we use for maintenance of upright stance during sensory conflict [129]. Along this theory, rats can be trained to solve tasks based on available sensory information and they appear to optimally integrate sensory information utilizing the PPC as part of the network required to resolve contradictions which require reweighting [130]. In their recent publication, Akrami et al. manipulated the neuronal activity of the PPC using optogenetic activation on 20% of trials in which rats were asked to integrate auditory sensory information to make correct forced-choice decisions. The group found that the PPC acted as a sort of historical log of the sensory information provided by previous trials. The authors suggested that the PPC is important in the processing of sensory history, and is helpful when using historical sensory input to guide current movement [130]. In small review of Akrami et al.'s article, Bitzidou dubbed this term, "cortical life-blogging[131]." This information reinforces Holmes and Spence's assertions that the PPC is involved in creation of the body schema[40].

A majority of dynamic sensory reweighting dysfunctions may be explained simply by sensory integration deficits, but there do appear to be some issues specifically within the component of dynamic sensory reweighting. Most investigations tend to support the notion that sensory reweighting is slower in healthy older people, according to a recent review by Saftari and Kwon [80]. Two investigations by Jeka et al, however, have suggested that there is no sensory reweighting deficit in healthy older and even healthy people who are fall prone [132,133]. The authors argue that their experimental design may explain the difference. In Allison et al.'s investigation, subjects were exposed to mediolateral oscillations of both visual input and light touch at various amplitudes. The group found that there was no difference in vision or touch gain between healthy older, fall-prone older, or young adults. All three groups showed similar evidence of effective dynamic sensory reweighting to changes in visual and somatosensory information [132]. This study was supported by the findings of Jeka et al [133]. In this investigation, healthy younger, healthy older, and fall-prone older adults were again compared by using visual displays which oscillated in the mediolateral direction, but added several mediolateral visual scene translation conditions as well.

The group found weak group effects, again casting doubt on the view that older adults are deficient in sensory reweighting [133]. Conversely, as mentioned earlier in this review, Eikema found that older people require more time to reweight sensory information and are less efficient at this process when exposed to a virtual reality environment [123].

Using tendon vibration to decrease proprioceptive reliability, Hay et al. observed increased sway in both younger and older individuals. Interestingly, only older adults were negatively affected when the tendon vibrators were turned off, re-establishing reliable proprioceptive information. The group used ten second alternating sequences in which tendon vibration was applied to the Achilles tendon and the tibialis anterior tendon. Additionally, the authors used prism-goggles to decrease visual feedback reliability. The group found that during the ten second "off" period of vibration, younger adults were able to re-establish baseline stability, while the older group was not. The authors concluded by stating this is evidence of diminished strategical flexibility of sensory processing and an inability to rapidly upweight sensory information once it is re-inserted [134]. This suggests inefficient reweighting in older individuals. These results are also supported elsewhere [135]. In their study, O'Connor et al. compared older and younger subjects who were exposed to a visual surround which rotated in the anterior-posterior direction at a consistent frequency but differing amplitude. The authors compared sway after cessation of the visual perturbation similarly to the investigation of Hay et al., and found that younger adults were again able to re-integrate reliable visual information more quickly than older adults after the end of visual perturbation, but older adults were able to eliminate the post-cessation of perturbation increase in sway after exposure to multiple trials. The habituation process appeared to require a greater number of trials and exposures to the perturbation in older adults, suggesting that aging increases the time-requirement for sensory reweighting [135].

On the opposite end of the age spectrum, investigations have shown young children are also inefficient at sensory reweighting [136,137]. Additionally, people with anxiety have reweighting dysfunctions and are resistant to downweight even inaccurate visual information [138]. Vestibular loss and stroke also leads to reweighting inefficiencies, due to a relative lack of options in their combination [139,140].

While many studies investigate how people are able to overcome and downweight unreliable sensory information, Eikema et al. took the opposite approach [141]. In their investigation, Eikema et al. used galvanic vestibular stimulation (GVS) during quiet stance with visual surround oscillations and/or Achilles tendon vibration. The group compared postural sway during GVS and no-GVS conditions between a young group and an older group. The authors found that during compared to the non-GVS condition, younger adults swayed less during GVS stimulation. This suggested that younger adults were able to successfully increase the relative weight of their vestibular system during GVS. Alternatively, older adults were unable to decrease their sway during GVS when compared the non-GVS condition. These results suggest that older individuals were less able to increase the weight of their vestibular system when provided GVS, which lead to an inability to decrease postural sway when provided GVS during periods of impaired visual and proprioceptive reliability [141].

Similar to sensory integration as a whole, fortunately, there appears to be a capacity for training of sensory reweighting to improve balance capabilities in several populations [142]. In their 2010 review, Anson and Jeka considered the efficacy of sensory reweighting training as a useful tool in the rehabilitation of postural control. As investigators have become increasing aware of the importance of sensory integration and sensory reweighting for postural control, they argued, behavioral interventions which account for reweighting are likely to be more successful than traditional approaches which only focus on the motor aspects of postural control [142]. These studies show the value in researching sensory reweighting, demonstrating that better understanding of the phenomenon can lead to improved rehabilitation paradigms.

Motor Adaptation

The product of multisensory integration and dynamic sensory reweighting is an ability to utilize the sensory system-based error signals in order to make improvements or adjustments to subsequent movements. This process, motor adaptation, involves updating of the body schema and is vital to successful movement within the world [29]. The study of adaptation is important both to understand the neurological basis of human movement and to understand the use of adaptation-based training in rehabilitation. Training adaptation and habituation in postural control has been found to help improve balance in those with disorders [143]. Understanding the process behind these adaptations may aid in the rehabilitative process to ensure that the adaptations are not maladaptive. Understanding the underlying processes behind adaptation may be useful in a broad range of cases including space flight, stroke, Parkinson's disease, dementia, traumatic brain injury and healthy aging [144–149].

Adaptation requires two effects. First, a gradual decrease in movement error after exposure to some sort of perturbation. Second, an after-effect, or error in the opposite direction once that perturbation is removed [150–152]. One classic example of motor adaptation by Gonshor and Jones showed a slow reduction in movement errors over days of wearing inverted goggles designed to flip the vision. After 27 days of inverted vision, the goggles were removed and a long after-effect persisted where the subjects had increased posture and gait errors for up to fourteen days [153]. The process of adaptation involves the sensation and perception of multiple sources of sensory feedback in order to identify differences between planned and observed motor outcomes. In order to adapt one must be able to interpret noisy and imperfect sensory feedback [152]. The rate of adaptation is related to the level of this noise or uncertainty [154]. Acerbi et al. shifted visual feedback during a task in which subjects were asked to identify the center of mass of a virtual object. Identification of an external object's center of mass is, they argue, a natural sensorimotor task. The researchers used two virtual disks connected with a thin line as the object which subjects were asked to estimate the COM of. Low-uncertainty trials included two disks of the same side, while high-uncertainty trials included differing sized disks. Additionally, the researchers added a random shift of visual feedback during reaching. The group found that while subjects were given unlimited time to correct their path based on the shift of visual feedback, they only corrected their movement during trials with low-uncertainty. The authors found that subjects only corrected their movement to the extend needed to avoid significant decreases in scores. The authors then concluded that subjects are more likely to use sensory feedback to make corrections when during times of higher movement certainty [154]. In addition to noise or reliability, our CNS is able to adapt preferentially to relevant stimuli [155]. Wei and Kording found that when presented with multiple visual stimuli, one containing relevant movement feedback and one containing irrelevant information, the CNS can essentially ignore error signals that are not relevant [155]. Eikema et al., in 2016, showed that motor adaptation can be facilitated or overridden when previously unavailable visual feedback is introduced. This feedback can override proprioception based adaptations due to increased relative gain [156]. Adaptation may also be task specific, as walking on an inclined surface may change pelvic alignment during gait but not during quiet stance, and may also preferentially aim to minimize temporal errors rather than spatial errors [157,158].

The movement adaptations we make are fundamentally important for successful movement throughout the world but successful adaptation can lead to maladaptive effects. For example, after a musculoskeletal injury, one's gait may adapt based on feedback of their new walking patterns. While the adaptation process may be intact, these adaptations may be harmful and lead to further issues [159]. One common gait dysfunction is asymmetry, which therapists often attempt to correct by promoting an adaptation towards symmetry by utilizing a split-belt treadmill paradigm [160]. In some cases however, asymmetry may have a functional purpose, and adaptation towards symmetry may be ill-advised [161].

Adaptation may be hindered in several populations. Children under the age of seven, for example, experience difficulty adapting to the new spatial relationship between the legs presented in split-belt walking [162]. Children with developmental discoordination disorder may have an even more difficult time, because they are over-reliant on pre-programmed control and less sensitive to feedback for adaptations [163]. Previous research has shown however that the most affected groups with the greatest motor adaptation deficits are those with brain damage [144,164–166]. Split-belt adaptation has been shown to be impaired after a traumatic brain injury [144]. Additionally, stroke, especially in the cerebellum lead to slower or impossible motor adaptations [164,165]. Because there are several populations with hindered adaptive capabilities, research into the scientific basis of motor adaptation as well as methodologies to increase adaptation capabilities is important to improve motor adaptation and therefore motor control in these disabled populations.

Neurological Basis of Adaptation

If brain damage is a major factor in adaptation deficits, it is important to understand the neurological factors behind adaptation in order to understand what brain regions, networks, and functions are most important for adaptation. As previously mentioned, the cerebellum is likely the most studied brain region in adaptation and has been shown to have a role in generating an "efferent copy" or the key which sensory feedback is compared to in order to identify error [155,167,168]. As such, the primary sensory areas, areas of sensorimotor integration and the cerebellum may serve as the network which produces the signals driving adaptation [155]. The PPC has been found to be an important brain area for sensory integration; Andersen et al, stated that the posterior parietal cortex (PPC) "sits at the interface between sensory and motor areas and performs sensorimotor transformations [38]." Based on this, the

PPC is likely an important part of the brain network involved in postural adaptation. Previously, lesions of the PPC have been characterized to lead to a “pure sensory stroke,” [47]. Derousne et al. presented a case study of an individual with functional sensations (e.g. pinpricks, light touch, heat, cold and vibration) but inaccurate positional senses. While this study provides additional weight to the PPC as a center for the creation of perception from sensory stimuli, it failed to identify if the subject had deficits in using sensory feedback to guide movement. A later study by Pause et al. found that posterior parietal lobe lesions lead to impairment of somatosensory and motor functions. In this study, Pause et al. used a testing battery to identify the effects of parietal lobe lesions. These measurements included sensory perception tests such as light touch sensation, vibration sensation and two-point discrimination of the fingertips as well as joint position sense of the finger joints, forearm and elbow. Patients also performed cube matching tasks in which subjects were asked to identify cubes hidden from vision to those on a photograph. Patients were also asked to maintain a static hand and finger posture with the eyes closed as well as maintain a consistent force on a strain gauge with and without visual feedback of force performance. The authors found that simple somatosensation such as light touch, vibration sensation or joint position sense was not impaired, but motor control tasks that involved sensory feedback such as the static position test and the consistent force generation test were significantly impaired. The authors concluded that the posterior parietal lobe is a necessary component of sensory processing for movement feedback [169]. More recently, neuroimaging data has confirmed that sensorimotor functions are disturbed with parietal lobe damage. The behavioral results are mostly apparent in goal directed motor behavior [170]. In their 2004 review, Andersen et al, suggested that the PPC is charged with the partial planning of movement and also comparing sensory input and the efferent copy arising from the cerebellum [38]. Their studies have shown that closed-loop control of aiming movement highly involves PPC neurons, showing the incorporation of sensory feedback in the PPC [171]. More recently, Andersen argued for the usefulness of studying the PPC in brain machine interface (BMI) investigation. Andersen argued that because the properties of neurons in the PPC, notably the intraparietal sulcus and superior parietal lobule are neither simply sensory nor motor neurons, instead possessing the properties of both, they are very useful for prosthetic control research. They argue that a BMI implant in the PPC would be able to encode sequential movements and sensory feedback [172]. In motor adaptation, Grea et al, also found that the PPC is part of the neural network which provides closed-loop feedback for online adjustments during aiming movements as well as decreasing error in between trials leading to adaptation [173].

Interestingly, the PPC appears necessary for the development of the body schema, and may be necessary for motor adaptations based on movement illusions to occur[174]. The authors performed experiments on healthy volunteers who had been screened and verified to exhibit postural adaptation during vibration. Somatosensory areas were activated by the tactile sensation of tendon vibration, but parietal areas were likely more important for the sensation of vibration-induced movement. The authors found that co-vibrating agonist-antagonist pairs led to somatosensory area activation without large PPC activation, but single-side vibration which lead to movement illusions led to greater PPC activation [174]. The authors concluded that parietal areas are necessary for the sense of kinesthesia. Similar results were repeated by Goble et al. who found that the PPC is activated by tendon vibration [175]. Based on the evidence, the PPC appears to reside in the functional space between sensory and motor functions and is an important structure in both the formation adaptations. In fact, Roll et al. found that there was disruption of cortical networks and activation in the PPC after hand immobilization through casting. Tendon vibration, however, prevented that cortical disruption. The group performed fMRI testing to study limb immobilization. They recruited sixteen healthy subjects who were immobilized via casting for five days. The cast prevented all hand and wrist movement but was built in a way to allow for proprioception and touch sensation. The experimental group received a treatment designed to mimic the sensations of movement (i.e. vibration) at the finger and wrist level. The researchers used fMRI during voluntary hand movements as well as tactile stimulation of the hand before and after the intervention. The group found disruption in the sensorimotor network functionality in the control group, who were immobilized and received no stimulation. Conversely, the group who underwent stimulation did not have any disruptions in their sensorimotor network, including the primary somatosensory cortex, PPC, and dorsal premotor cortex. These results show that sensory stimulation is sufficient to maintain sensorimotor cortical functionality even when actual movement is blocked. The authors conclude that these results indicate a possibility of maintaining sensorimotor network functionality during rehabilitation even if movement is impossible. Tendon vibration avoids disruptions by lack of movement, that may suggest that the PPC is among the primary locations for motor adaptation in response to these types of interventions[176]. A series of investigations performed by Naito et al. have highlighted the role of the inferior parietal lobule (IPL) in the development of proprioceptive adaptations. The IPL is one of two major components of the posterior parietal cortex (PPC) and lies at the nexus of the audio, visual, and somatosensory cortices[177]. In their 2016 review, Naito et al. wrote that the IPL is connected to the inferior frontal cortex via the inferior branch of the superior longitudinal fasciculus, and that this network is recruited during motor adaptation. This activation is likely related to body-awareness and uses sensory information to update the internal representation of body positioning[178].

In one of the group's earlier investigations, Naito et al. utilized fMRI in order to compare cortical activation during four conditions. During the first condition, the hands were immobilized and tendon vibration was performed on the extensor carpi ulnaris of both hands separately. The group next performed vibration on the processus styloideus ulnae, in order to achieve a similar skin-sensation without a chance of vibration-induced movements. The group found that the supplementary motor area, cerebellum, and bilateral IPL were activated during the actual tendon vibration, but not the bone vibration. The right IPL was however activated to a greater extent than left regardless of which arm was vibrated. As a result of this investigation, the authors suggested that the perception of movements in response to vibration engages the right IPL. Next, the group was interested to identify how their earlier findings extended to the lower limbs. After performing tendon vibration on distal tendons in the hands and feet, the group found that right IPL activation was the greatest common factor between upper and lower body bilateral stimulation[179].

A recent study by Manuweera et al. found that the right IPL is also selectively activated during virtual reality mirror illusion feedback, suggesting that the IPL's and PPC's role in motor adaptation is not limited to vibration[180]. Kito et al., in 2016, found that the after-effects of vibration likely depend on cortical processing of the initial illusion. While they only measured motor cortex excitability using TMS, the group suggested that cortical activation during adaptation interventions is necessary for an after-effect. The results of these investigations are important, as they provide evidence that excitation of the IPL and PPC are necessary for adaptation, and likely aftereffect as well. Based on this, neuromodulation of the PPC may lead to alterations in response to an intervention such as an incline-intervention designed to elicit lean after-effect

Stimulation such as that described by Roll et al. uses a periphery-centric methodology to maintain cortical functionality. Recently, the popularity of neuromodulation research has increased substantially. Conversely to Roll et al., neuromodulation techniques involve stimulation of the CNS directly.

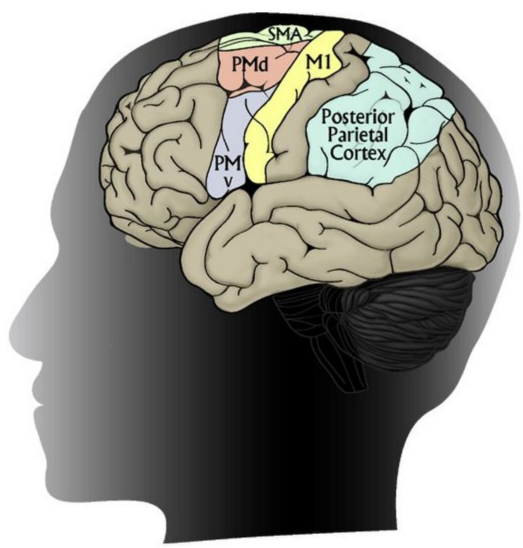

Fig 3. Choi (2006) highlighting the location of the PPC

Neuromodulation

A large portion of early studies regarding neurological dysfunctions in movement as well as movement adaptation have utilized clinical populations such as those with Parkinson's disease (PD) or stroke. Work understanding these populations is of paramount importance, and much of the research that occurs in this area is aimed towards rehabilitation of these populations. However, directly studying people who have had a stroke or those with PD is not without drawbacks. First, there is a limited potential subject pool that may be studied. Second, their fitness may be limited to the point of an inability to perform certain experiments. Third, the symptoms of individuals who have suffered a stroke or have Parkinson's disease are unique and exists along a continuum making comparisons within small groups of subjects problematic. For these reasons, neuromodulation techniques have been recently utilized as a tool to study the inhibition or excitation of certain brain regions in order to identify outcomes on behavior. While not a perfect analogue, neuromodulation through transcranial direct current stimulation (tDCS) or transcranial magnetic stimulation (TMS) can serve as a method to approximate lesions [44,181].

The basic mechanism of TMS involves Faraday's principle of electromagnetic induction, which shows that electric current passed through the brain can elicit neuronal activity [182]. TMS is non-invasive and can be applied to cortical tissue as well as spinal cord and even peripheral nervous tissue [183]. Single pulse TMS uses a large current intensity delivered in a short period of time, sufficient enough to directly induce action potentials, which can be used to measure the magnitude of stimuli necessary to induce a response [183]. Repeated TMS or rTMS has high spatial and temporal resolution and is able to influence plasticity for an acute period [184].

The principal difference between TMS and tDCS is the current density. As noted earlier, TMS delivers currents that are sufficient to create action potentials. Conversely, tDCS provides subthreshold currents, which are also lower in spatial resolution [185]. Transcranial direct current stimulation involves the transfer of current between anodal and cathodal electrode(s). These electrodes are placed on the cranium in such a way that the current passes through the desired tissue, which can lead to the modulation of cortical excitability [186]. Multiple exposures to tDCS interventions can also lead to changes in longer term plasticity [187]. While tDCS does not provide a current sufficient to directly cause action potentials, research has shown that tDCS can modulate cortical excitability. This has been demonstrated using fNIRS, TMS and EEG measurement techniques [43,44]. Zheng et al. demonstrated through fMRI that anodal (positive) brain stimulation leads to increased cerebral blood flow during stimulation and cathodal (negative) stimulation leads to a decrease in blood flow following stimulation. They also show other areas are affected suggesting that tDCS can not only modulate regional brain activity but also functionally linked brain areas in network [44]. There are advantages of tDCS over TMS, including cost and portability. Administration of TMS requires relatively expensive coils as well as specific computing software. Conversely, tDCS devices available commercially on the market are much less expensive. Additionally, TMS is most often administered while the subject sits motionless in a chair in a laboratory setting, while tDCS administration can theoretically occur almost anywhere. Both of these factors make tDCS a more attractive option for researchers who have limited funding or wish to perform stimulation in a wider variety of settings. Neuromodulation techniques have also been used to study motor adaptation. Using tDCS over the cerebellum, Jayaram et al. were able to alter initial spatial adaptation to a split-belt walking paradigm. [188]. Doppelmayr et al. also found that cerebellar tDCS affects motor adaptation [189].

Neuromodulation of the posterior parietal cortex (PPC) has furthered the early understanding provided by the lesion studies mentioned previously in this literature review [47,169]. Transcranial magnetic stimulation of the PPC has led to disruption of sensory feedback based path corrections within trials during reaching [190]. Using neuromodulation to disrupt the PPC, the group repeated the findings of earlier lesion-based papers, that the PPC was involved in sensory based error computation. This highlights the usefulness of neuromodulation as a loose analogue for lesion studies [169,190]. Reaching tasks appear to be the most studied with regards to PPC neuromodulation. As previously mentioned, disruption of the PPC leads to impaired path corrections during reaching trials. Furthermore, disrupting the PPC by use of TMS hinders adaptation of reaching trajectories between trials when there is an induced perturbation. The lack of decrease in error trial to trial highlights the PPC as a target for motor adaptation and suggests sensory feedback, integrated in the PPC, may be used in network by the cerebellum to reduce error [191]. Additionally, cathodal tDCS over the PPC led to proprioceptive drift during reaching tasks when vision is removed. Individuals who had underwent cathodal stimulation had impaired perception of position and movement during reaching tasks when vision was removed. The authors suggested that this was an impairment of sensorimotor representation and lack of ability to correct movement errors [42]. Additional studies have demonstrated that neuromodulation of the PPC leads to alteration of sensory integration capabilities [41,45]. Motor adaptation is important for studying the mechanisms proprioceptive integration and will be the subject of further discussion throughout this literature review. Bruno et al. recently reported that tDCS of the PPC alters the perception of motor illusions. In their experiment, Bruno et al. performed anodal or cathodal tDCS over the premotor cortex or the PPC. After this, they delivered a motor monitoring task, where they were tasked with verbally reporting whether or not their hand twitched in response to a TMS pulse designed to induce twitching. They found that stimulation of the premotor cortex did not alter perception of hand twitches but stimulation of the PPC did. Cathodal stimulation of the PPC increased the feeling of phantom movement illusions (i.e. subjects reported a twitch that did not actually occur). Anodal stimulation increased the rate of false-negatives (i.e. the subject did not report a twitch that actually did happen) [46]. Using more invasive methodology, surgical manipulation of the PPC can prevent initiation and execution of voluntary movements entirely [192]. Neuromodulation of relevant brain regions for motor adaptation is an emerging and increasingly popular field. While these techniques are not a perfect analogue for disease models, they do offer advantages in subject recruitment and allow for more uniform stimulation to be performed, in contrast to the high individuality between people with stroke, PD, or other neurological disorders. Thoughtful use of neuromodulation should continue to inform our understanding of the CNS's role in motor adaptation and sensorimotor control in general. This section has demonstrated the effects of neuromodulation on motor adaptation, but there is insufficient understanding to this point considering the effects of neuromodulation on postural adaptation.

Postural Adaptation

Postural adaptation is based on the same characteristics as general motor adaptation. When exposed to changes in in the environment, the CNS will utilize sensory feedback in order to evaluate movement errors in an attempt to gradually reduce errors back to baseline. This adaptation reflects updating of the body schema. Postural adaptation is an important avenue to study humans have to undergo this process constantly as they move within their environment and are exposed to different goals, surface or visual conditions, or any number of other changes in the environment. Researching these phenomena is not only important in understanding poor postural control in disabled populations but also in better understanding the process of adaptation. Currently, questions are being proposed seeking to answer whether or not inter-context motor adaptability is a skill that can be trained. Does training gait or reaching adaptation improve postural adaptability? Are some people inherently better adaptors than others? Some studies seem to suggest that training can improve the general ability to adapt, and adaptability may be indeed a transferrable skill [193].

One of the most popular ways to study postural adaptation is based on tendon vibration of the shank muscles. Vibration of the shank muscles, including the gastrocnemius, soleus, and tibialis anterior, is generally applied with motorized devices placed around the distal tendon of the muscle [194]. The vibration may be applied between a wide range of frequencies and amplitudes, but 80-100Hz with an amplitude of 1mm appears to be a largely accepted vibration protocol [195–198]. Tendon vibration is known to decrease proprioceptive reliability, requiring dynamic sensory reweighting in favor of visual and vestibular signals in order to maintain postural stability [23]. Because of this, tendon vibration is an effective tool in researching dynamic sensory reweighting. Hwang et al. demonstrated this phenomenon in their investigation by applying 80Hz vibration to the Achilles tendons while also performing visual and/or vestibular perturbations through a moving visual stimulus as well as galvanic vestibular stimulation. The authors found that moving the visual support increased proprioceptive weight, unless vibration was being concurrently applied. During these periods, the decreased reliability of the proprioceptive system forced a higher reliance on visual and vestibular signals despite the moving visual surround [23]. Kabbaligere et al. performed an experiment to further identify the process of multisensory integration by using a combination of tendon vibration and a rotating visual field and measuring the effects on COP displacement as well as postural stability. The group identified that the sway elicited by the combined perturbations was not equal to the sum of displacements provided by each of the perturbations when separate. They suggested that this gave greater insight to dynamic sensory reweighting and showed that multisensory integration likely utilizes a weighted combination process based on reliability, not a basic summation of individual cues [120]. Other researchers have also identified vibration's influence on the recovery from postural perturbations [121]. Postural stability appears to recover to baseline levels after several minutes of tendon vibration [199]. Results such as these do not cast doubt as to the effectiveness of tendon vibration to reduce proprioceptive reliability, but instead highlight the ability for dynamic sensory reweighting. As mentioned earlier, older adults tend to have sensory reweighting deficits. Vibration studies have supported this finding as well. Downweighting of proprioception during postural control tasks when exposed to vibration appears to be slower in older adults [198].

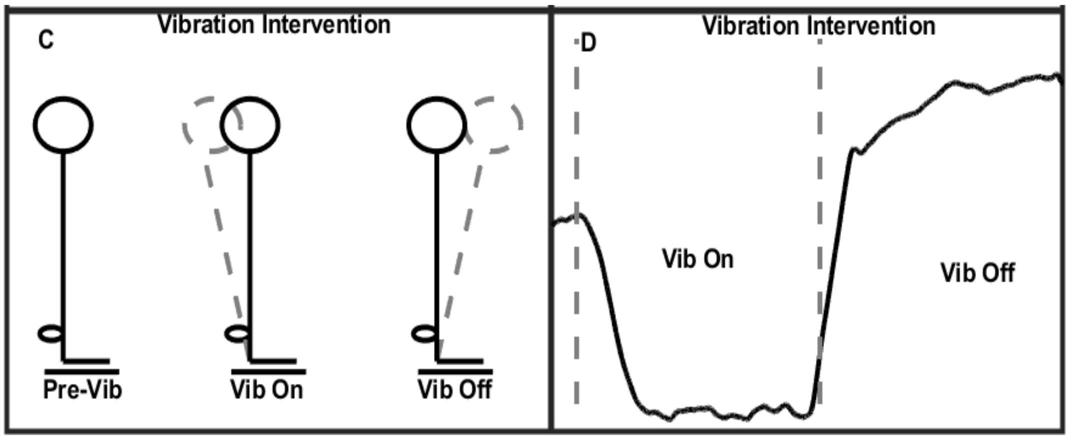

Fig 4. Left: Schematic representation of a bout of Achilles tendon vibration (Vib On) and after-effect (Vib Off). Grey indicates typical changes in position. Right: Representative trial of the effects and after-effects of Achilles tendon vibration

Tendon vibration is also known to induce movement in the direction of vibration. These movements were described by Goodwin et al., in 1972, where they wrote that tendon vibration leads to movement in the same direction as the vibration, and that these movements are likely based on increased firing rate of muscle spindles leading to a perception of muscle stretch which is not actually occurring [24]. These findings have later been reinforced by several studies including Roll and Vedel (1982) where they concluded muscle spindles are related to vibration-induced movement[200].

Thompson et al. expanded on these results when they measured whole-body kinematics as well as kinetic and muscle activation data during Achilles tendon vibration. The group found that despite the ankle-only stimulation, there were changes in whole-body postural orientation. They found increased extension in the trunk as well as the lower limbs. These results suggest that vibration-induced movement is a global phenomenon, not limited only to the joint to which they are applied [201]. Even when one is attached to a backboard, removing any equilibrium constraints and making a perceived stretch of the Achilles tendon irrelevant to fall risk, tendon vibration still results in a perception of movement and people will shift backwards in a fashion similar to when standing freely [194]. Vibration does lead to adaptation, but as a form of motor adaptation, there are also observed after-effects from vibration [25]. Wierzbicka et al. found that even thirty seconds of tendon vibration is enough to cause a postural after-effect in the opposite direction of vibration. They found that Achilles tendon vibration led to a posterior shift in the COP, and when vibration was stopped there was an anterior shift of COP that surpassed the baseline value. The group found the opposite during tibialis anterior vibration, which led to an anterior displacement during vibration and, in some subjects, a posterior after-effect.

A majority of studies which investigate dynamic sensory reweighting during postural control utilize manipulations or perturbations of one or more systems (e.g. tendon vibration or sway-referencing for proprioception, sway referencing or prism goggles for vision, galvanic vestibular stimulation or supine position stance for the vestibular system [202]). While these studies are critical for understanding intersensory reweighting in postural control, relatively fewer studies however have sought to identify intrasensory reweighting dynamics. This leads to the question: What happens if one perturbs two sources from the same channel? Hatzitaki et al. instead used one continuous proprioceptive manipulation, vibration, and one transient, dynamic support surface tilting. Healthy subjects were tasked with performing six conditions. Each subject performed a quiet stance condition with and without Achilles tendon vibration. They also performed conditions in which their support surface unexpectedly tilted in the toes up or toes down direction, with and without vibration. The group found that during quiet stance, vibration led to a posterior shift in the COP as well as decreased stability, which is consistent with the general consensus of the literature. During the trials with support surface rotations however, the effect of vibration was muted. There was no corresponding increase in instability nor shift in COP position. These results suggest that the CNS can ignore some proprioceptive information while still responding to other information. The proprioceptive stimulation of vibration was downweighted, but the stimulation of support surface rotations was not. This is among the first studies to demonstrate intrasensory reweighting and shows the flexibility of the CNS when being exposed to multiple perturbations [203]. In a follow-up study from the same laboratory, Doumas et al. performed another experiment using multiple proprioceptive manipulations. The group performed a postural control stance in which subjects stood quietly for two minutes, followed by three minutes of Achilles tendon vibration and/or a sway referenced support surface and another three minutes of quiet stance in order to measure after-effects. Unsurprisingly, the group found the greatest sway amplitude early in the intervention trial when the two manipulations were combined, but as subjects approached the end of the intervention during the sway-referencing only condition, their instability decreased. Regardless of intervention (vibratory, sway-referenced, or both) after-effects were present but the subjects returned to baseline within twenty seconds of the end of the intervention. This confirms that reweighting occurs independently of the type of manipulation, as the proprioceptive system was upweighted over the course of twenty seconds regardless of which intervention was used [204].

Lean After-Effect

Another emerging form of postural adaptation is the study of lean after-effect (LAE). This methodology was first described by Kluzik, Horak, and Peterka in 2005 [31]. Lean after-effect is formed when a subject performs some task such as standing, walking, or marching while on an altered support surface. The classic example found in Kluzik et al. 2005 utilized quiet stance while on an inclined (i.e. toes up) platform. During an incline-intervention, the subject typically immediately oriented themselves vertically with respect to gravity, leading to little change in the center of mass (COM) but a change in the sagittal plane ankle angle throughout the incline-intervention. After 2.5 or more minutes, the subject was returned to a horizontal support surface. At this time the subject may or may not have presented LAE, which is a relatively long-lasting adaptation in which the subject’s center of gravity (COG) and COP. These after-effects last for several minutes before slowly dissipating back towards their baseline positioning. Kluzik et al. found that roughly 60% of their subjects were “responders” while the remaining 40% did not exhibit a LAE [31]. Subjects tended to be aware that they were leaning forward but expressed that it “felt natural.” Later, several studies have found that a majority (56.5-85%) of healthy individuals respond to incline-interventions but some subjects some do not exhibit any forward leaning [27,30,205]. Some others have found LAE responses in every subject [206].

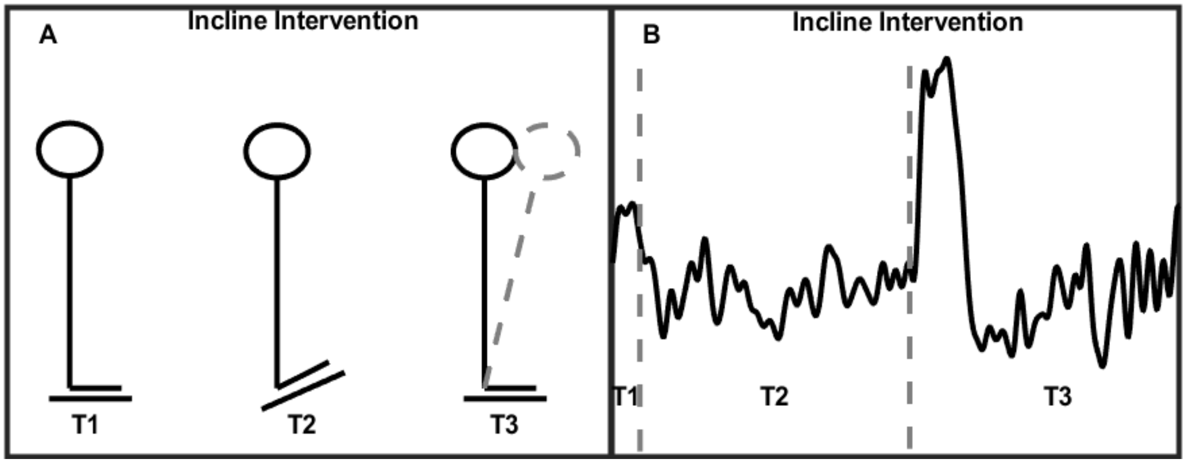

Fig 5. Left: Schematic representation of an incline intervention and after-effect. Grey represents typical shift in position. Right: Typical responses during (T2) and following (T3) an incline-intervention.

The aforementioned article highlights their reason for beginning the line of LAE research. When one stands on a horizontal surface, there is little way to discern the components of their postural orientation. The visual, vestibular, and proprioceptive systems all provide congruent, accurate, and reliable information. When the support surface is inclined, however, there is an alteration in the relationship between the gravitational vertical and the support surface. These results are conditional on at least two factors. First, the absence of visual feedback. If the subject is allowed visual feedback, the LAE phenomenon will quickly dissipate [128]. Second, the subject should be primed not to resist the LAE. Typically, instructions such as, "Stand in a relaxed way… try not to pay attention to your posture and do not resist any pull or tendency to lean," are given so that subjects do not actively attempt to re-orient themselves with gravity. The authors suggested that if an individual maintained a similar kinematic profile when they returned to horizontal (i.e. increased ankle dorsiflexion), that individual likely used a somatosensory/proprioception dominant sensory integration strategy. Conversely, if the individual exhibited an immediate re-orientation towards gravitational vertical, that individual likely used a vestibular graviception based sensory integration strategy. The investigation hoped to identify whether or not LAE responses existed on a continuum or if two groups (somatosensory/proprioception dominant and vestibular dominant) could be identified. Their results indicated that there was not a continuum of responders, but instead two dichotomous groups were identified.

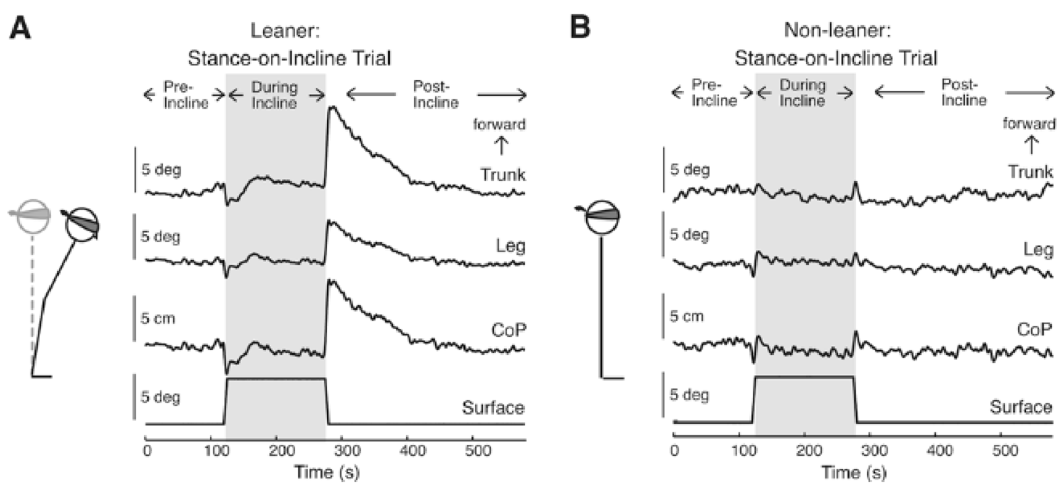

Fig. 2a, b Post-incline postural effects for a leaner and a non-leaner. Sagittal plane CoP and kinematic data are from individual trials. The *shaded area* indicates the time period during which the surface was inclined at 5° toes-up. **a** The long lasting forward lean of the whole body after stance on a toes-up inclined surface in a representative subject who leaned. **b** The upright postural alignment adopted throughout the trial for a representative subject who did not lean

Fig 6. Kluzik (2005) depicting the difference between responders (dubbed Leaners) and non-responders (dubbed Non-Leaners)

Kluzik et al. (2005) also investigated the reliability and repeatability of LAE phenomena. Responders to the incline-intervention were exposed to additional trials days or weeks later and it was found that LAE duration and maximum forward lean exhibited interclass correlations of 0.95 and 0.85, respectively. This demonstrated that re-administration of incline-interventions are an appropriate method of studying postural adaptation, as results are consistent within days and weeks [31]. In fact, later studies would test subjects up to nine total times, including four times per day without finding diminished results due to habituation or learning [128]. The initial investigation was informative of both the dichotomous response to a toes-up intervention as well as to the repeatability of the intervention, but several questions lingered.

1. Do responders respond due to local changes such as alterations in muscle spindle activity from prolonged increases in ankle dorsiflexion, or are the changes central in nature?
2. What populations may have differing responses to incline-interventions, and why?
3. What co-interventions can be done to augment or mute LAE responses, and what would be the mechanism behind this alteration?

Several investigations have been undertaking since this 2005 report in order to answer these questions, but still more work needs to be done.

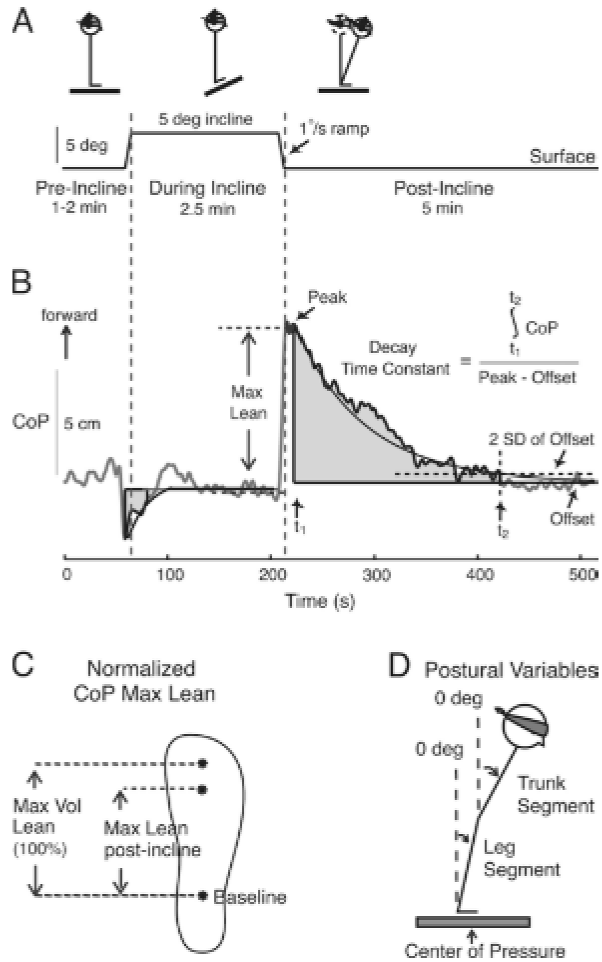

Fig 7. Kluzik (2005), depicting the typical outcome of a responder to an incline-intervention

In a follow-up study, Kluzik, Horak, and Peterka (2007) aimed to determine whether LAE is a peripheral adaptation based on muscle spindles in the gastrocnemius or a central adaptation based on some sort of internal recalibration of the preferred frame of reference [207]. In order to answer this question, the groups compared a group of subjects' LAE after two tasks. The control task was the classic incline-intervention, a baseline, an incline-intervention of 2.5 minutes, and a post-test on a horizontal surface. The experimental task was the same intervention, except subjects were instructed to march in place during the incline-intervention. The authors chose this intervention because while a static stance incline-intervention resulted in a constant ankle angle, marching in place leads to a dynamically changing ankle angle. During the intervention, when subjects stood, they tended to orient themselves vertically, while during marching subjects leaned forward. Despite this, LAE was similar between the two conditions. Because postural orientation during the incline-intervention differed, as well as the joint angles due to marching, the authors suggested this means LAE is a central phenomenon. Based on the after-effects they believed LAE is caused by a global postural variable related to the orientation of the whole body. The authors believed that the relationship may be between the trunk orientation and the support surface orientation [207].

In order to test their theory that LAE is caused by central modifications and that the relationship between trunk orientation and the support surface, the authors performed two additional experiments [26]. Subjects were first tasked with undergoing incline-interventions of different amplitudes. The authors hoped to identify whether there was a linear or other relationship between the incline-intervention angle and the LAE magnitude. Second, the subjects underwent an experiment in which they underwent incline-interventions and were ether free to move during the post-test (i.e. the basic incline-intervention) or were blocked from moving forward at the level of the hips. During the second condition, subjects were unable to lean forward at the ankle joint. The results of the first experiment supported the earlier hypothesis that the trunk to support surface relationship is the dominating factor in LAE. The authors found that regardless of incline-magnitude (2.5-10 degrees), post-test ankle angles were similar.

Beyond 5 degrees, COM saturated and did not further increase. A majority of changes in LAE beyond an incline angle of five degrees were observed in the trunk angle. This may be due to stability requirements to maintain the COM inside of a certain value to prevent falling. Because the trunk angle is not so strictly constrained for postural stability, only the trunk was able to incline further. The authors suggested that this is further evidence for their hypothesis. Only the trunk angle was sensitive throughout the entire range of incline angles, supporting their hypothesis that the global variable leading to LAE is the trunk to support surface relationship. Results from their second experiment further support this hypothesis. They showed that blocking movement at the hips during the post-test did not abolish LAE. Despite the fact that during the incline-intervention, only the ankle angle is changed, LAE persisted even when ankle movements were blocked during the post-test. The trunk inclination during the post-test with blocked lower body movement further supports the trunk to support surface relationship hypothesis. This investigation provided strong additional support to the notion that LAE is in no way a local phenomenon and must be centrally processed, likely through a variable aiming to maintain a relationship between the trunk angle and the support surface. This variable may be quasi-represented by center of mass, since the COM is anatomically located near the navel [26]. The work of Kluzik, Peterka, and Horak seem to strongly suggest that LAE is indeed a global phenomenon likely based on the relationship between the trunk and support surface angles. This, to some extent, has answered the first question which arose from the initial study: Do responders respond due to local changes such as alterations in muscle spindle activity from prolonged increases in ankle dorsiflexion, or are the changes central in nature? Further research was needed to answer the other questions which arose.

Based on the original article, two groups of people emerged from incline-intervention experiments, responders and non-responders [31]. They argued that this is based on whether the subject employs a proprioceptive or vestibular dominant strategy. This leads to the question, are certain populations more or less likely to respond? Nashner argued that humans select the most appropriate, optimal combination of sensory feedback for the given action [119]. We know that some people who have had strokes, as well as people who have Parkinson's disease and even those healthy aging lead to diminished somatosensory function [66,68,70]. We also know that vertigo and other vestibulopathies are common in the elderly [89]. Additionally, there are changes in sensory dominance that correspond to several disabilities as well as healthy aging. Wiesmeier et al. found that elderly people use a proprioceptive dominant strategy more often than trusting visual or vestibular cues [208]. Based on those understandings, it is natural for researchers to use clinical populations to investigate LAE to attempt to further explain the difference between responders and non-responders.

Recently, Chong et al. compared the LAE of twelve people with vestibular disorders as well as twelve age-matched control subjects. They aimed to identify if vestibular patients would produce a somatosensory dominant (i.e. present LAE) response to an incline-intervention. The group hypothesized that the vestibulopathy group would exhibit a somatosensory dominant response, due to the chronic weakness of their vestibular system. Because of their vestibular disorders, it can be hypothesized that these individuals tend to rely more on somatosensory feedback. Each group performed an incline-intervention as well as a SOT. As noted previously, the SOT is comprised of six conditions which systematically alter proprioceptive information and alter or remove visual information, leading to an isolation of the vestibular system [27,110]. The vestibular group in this experiment followed the classical pattern of poor performance when the proprioceptive and the visual systems are both unreliable. Furthermore, the vestibular group experienced a LAE incidence of 100%, while in the control group only 58% of subjects experienced LAE. These results reinforce the notion that LAE is dependent on the relative weighting of the somatosensory and vestibular systems. Furthermore, Chong et al. mentioned that these stimuli may lead to adaptation through habituation. Repeatedly administering somewhat aggravating stimuli can decrease symptoms of vestibulopathy, so if a patient is able to tolerate a protocol like an incline-intervention, there may be rehabilitative use [27,209].

Another experiment led by Chong sought to identify the effects of PD on LAE development [205]. As mentioned previously, PD leads to somatosensory dysfunction [68]. This may lead to a speculation that due to decreased somatosensory function, a vestibular-centric strategy may be used and LAE may not be exhibited in these patients. In an attempt to test that, Chong et al. compared young and older healthy adults as well as PD patients during an incline-intervention with and without augmented tactile light touch feedback. Chong et al. used this approach because previously Dickstein, Peterka and Horak found light touch may improve central integration of proprioception, which is likely defective in PD [205,210]. Results from Chong et al.'s study revealed that light touch had little effect on the healthy young and healthy older adults, but increased LAE responder rate significantly in PD patients. This suggests that light touch lead to dynamic upweighting of somatosensory information because it provided augmented somatosensory feedback. A group of people with somatosensory dysfunction who increased their LAE after receiving augmented somatosensory feedback further supports the notion that the phenomenon of LAE has a relationship with the relative weighting of proprioception [205]. Chong et al., in both 2014 and 2017 investigated sensory impairments and their effects on LAE.

The third question promoted by Kluzik et al. 2005 was: What co-interventions can be done to augment or mute LAE responses, and what would be the mechanism behind this alteration? In 2010, Earhart et al. investigated the effects of the introduction of visual feedback on the recovery from LAE [128]. It had been previously established that the eyes must be closed for LAE to form, so Earhart sought to systematically change the availability of visual feedback in order to identify the precise effects on LAE [31,128]. The investigation utilized one subject population who underwent four conditions. The four conditions included the basic incline-intervention, an incline-intervention in which the subject opened their eyes throughout the post-test, and two conditions in which the subjects were instructed to open their eyes only for one or two designated twenty second periods. The authors confirmed that visual information rapidly canceled LAE. During the vision condition, LAE was not found. During the two conditions in which visual information was only temporarily provided however, LAE was merely interrupted. When told to open their eyes, the subject immediately returned to a stance that was upright with respect to gravity. When instructed to re-close their eyes, the subject returned to a leaned stance. This information, the authors suggested, shows that vision does not immediately alter the interpretation of somatosensory information. Instead, the vision acted as an extrinsic reference frame. When vision was re-introduced, it was immediately upweighted to overcome the incongruent proprioceptive feedback. When the eyes were closed, however, the recent memory of a proprioceptive vertical was re-instated as the dominant factor behind the postural strategy [128]. These results suggested both that visual information was indeed sufficient to completely overcome the LAE, but also that LAE can be affected by dynamic sensory reweighting when additional information is presented or removed [128].

While Earhart et al. identified differences in LAE based on dynamic reweighting by systematically altering the presence of visual feedback, Wright et al. followed the path set by Hatzitaki et al. and sought to identify differences in the development of, and de-adaptation away from LAE based on proprioceptive perturbations [203,206]. The group recruited healthy subjects for two experiments. First, the subjects were compared on two incline-interventions. For the first condition, the basic incline-intervention was used. For the second condition, the platform was rotated at a frequency of 0.25Hz between amplitudes of 4-10 degrees during the incline-intervention. This provided a period of inclined stance but did not provide a static ankle angle or postural orientation. Results from this experiment showed that a sinusoidal tilting incline-intervention led to LAE that was not different from a static position. These results showed that a fixed position is not important, which extends the arguments made by Kluzik et al.'s investigation where LAE was still identified after a bout of marching on an inclined surface [207]. The advantage of this investigation stems from the fact that the subject's task has not changed, instead of ensuring a non-static ankle angle through marching, this investigation ensured a non-static ankle angle through a tilting support surface. In their second experiment, Wright et al. modified the post-test criteria. After performing an incline-intervention, subjects were either exposed to a stable support surface during the post-test, or a sway-referenced support surface. The authors found that sway referencing led to fast abolishment of LAE and posterior shifting of the COP. Sway-referencing the support surface is known to decrease proprioceptive reliability, leading to increased weighting of the vestibular system concurrent with downweighting of the proprioceptive system [198,211]. It is likely that the sway-referenced condition led to decreased proprioceptive weighting, which is believed to be related to absence of LAE [27,31].

Overall, lean after-effect research provides a useful platform to study postural adaptation. This line of research is useful for multiple reasons. First, these interventions can help identify the dominant sensory system in an individual [27,31]. Second, there is potential for their use in rehabilitation [27,30,205]. As explained by Chong et al. in 2017, incline-interventions can serve these two functions well. In vestibulopathic individuals, performing an incline-intervention and identifying LAE is a possible method for identifying how successfully the patient has compensated for their vestibular loss by upweighting somatosensory inputs, which can inform the clinicians for training strategies moving forward. For training, Chong et al. discusses the possibility of using incline-interventions as an aggravating, adaptation inducing stimulus. Repeated exposure to these stimuli may decrease the patient's symptoms and improve balance in a process called adaptation through habituation [212] . This process may condition poorly-compensated vestibulopathic individuals to utilize their somatosensory system to a greater extent. There is no reason to expect that these ideas would not extend to other populations with sensory deficits. There are many possibilities for further exploration in this line of research.

Use of Technology in the Literature

A majority of the literature discussed in this review use laboratory equipment to compare various groups or conditions. For the purpose of this review, the two most important pieces of technology are force plates and motion capture systems. Their use in posture and gait research is near ubiquitous in recent years and allows for precise and robust comparisons to be made.

Force Plates

Force plates record ground reaction forces which are exerted during a subject's contact with the plate. They are able to measure at a high frequency, typically around 1000Hz, and can measure forces in three planes [213,214]. These measurements are often used to calculate center of pressure (COP), which is a two-dimensional representation of the averaged sum of forces exerted onto the force plate at any given moment [214]. Often during posture and gait research, especially that which involves treadmill walking, two separate force plates will be used [215]. This provides advantages in obtaining separate COP recordings from each force plate as well as allowing for greater identification of gait events, and simple calculations can be used to combine the data from two force plates into a single COP [214].

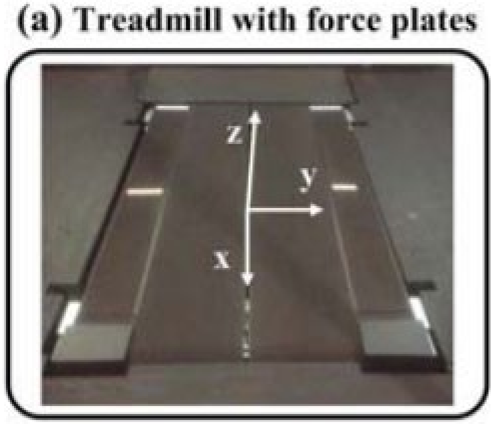

Fig 8. From Lee et al. 2017 depicting force plates [215]

Force plates have been used in a majority of previous lean after-effect (LAE) research [26,30,206]. These investigations used force plates to measure the presence and magnitude of LAE after an incline-intervention. Several experiments have used force plates to identify maximum COP in the anterior direction during post-test after an incline-intervention [26]. These measurements can be expressed as an absolute measure of the anterior shift, in centimeters, of the COP during the post-test. Alternatively, the measurements can be normalized to a previously administered limit of stability test in order to normalize LAE to a percentage of maximum voluntary lean [31]. While a majority of LAE research has not focused on postural stability measures, force plates are also useful in measuring postural stability [120].

Motion Capture

Kinematic analyses through motion capture systems are another popular tool in biomechanics and motor control research. In some investigation, motion capture is performed using active transmitters which use inertial measurement units (IMUs) [120,216]. The gold standard and most common, however, is use of passive markers and infrared cameras including the Motion Analysis System or the Vicon motion analysis system [26,207,217,218].

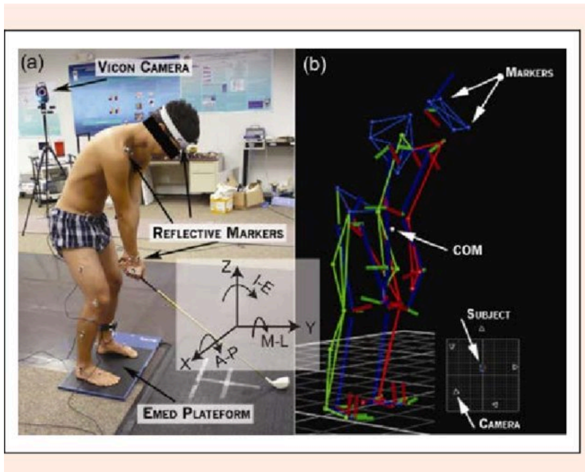

Fig 9. From Najafi et al. depicting motion capture system [219]

Kinematic analyses using motion capture are relatively less common in posture research than gait or other motor control experiments because often, researchers believe that relevant data can be sufficiently captured by the force plates, making motion capture unnecessary. Kinematics however can be useful in lieu of or in addition to force plates. Motion capture technology has been used in many postural control studies [23,216,220]. Additionally, several LAE experiments have utilized motion capture. Motion capture is necessary in order to measure the relative contributions of the sagittal ankle angle and trunk angle to LAE. Furthermore, motion capture allows for the calculations of center of mass and center of gravity which can be used instead of or even compared against center of pressure data [26].

Neuromodulation using tDCS

Transcranial direct current stimulation (tDCS) has been employed in the literature for over twenty years. Recently the popularity of tDCS as a useful tool in the alteration of cortical excitability has increased however. Mild irritation and some contra-indications are often reported in the literature, leading to a necessity of some additional exclusion criteria for participation in tDCS experiments [221]. In general, however, several large scale reviews have found tDCS research to be safe [222,223]. This technology effectively alters cerebral blood flow and can hypo or hyperpolarize underlying neurons to increase or decrease cortical excitability [222,224]. This technology has recently became popular in posture research [225–230].

Digital Signal Filtering

Biomechanics and motor control research employing force plates and motion capture systems often utilize low-pass filters set to pass frequencies below five or ten Hz. Above this frequency, the contributions of actual movement to signal are minimal and mechanical noise tends to dominate the signal. Filtering allows for the minimization of noise and the maximization of useable signal [26]. Low-pass filters of this nature are often used to measure postural stability as well as relevant gait factors include the adaptive variables that have been listed above [120,158,231]. Lean after-effect research is somewhat peculiar in that many experiments do not use, or at least do not solely use low-pass filters with cut-off frequencies between five and ten Hz. Lean after-effect studies may compare postural stability between conditions but tend to be more interested in mean positioning of the center of pressure or center of gravity irrespective of postural sway. Because of this, LAE experiments endeavor to filter out actual movement signal that is captured in the range which typically encompasses postural sway (e.g. between 0.1 and five Hz) [31]. In order to obtain mean and maximal values in positioning, represented by COP, COG, and joint angles that have not been contaminated by postural sway, researchers began to employ ultra-low-pass filters with cut-off frequencies of 0.1Hz. This allows for the identification of a "chosen" mean positioning which can be compared between conditions [26,31,207]. Utilizing this methodology, researchers are able to process the data in two ways in order to quantify both LAE and postural stability. The researcher can quantify LAE using the ultra-low-pass 0.1Hz filter and can quantify postural stability using a band-pass filter which passes frequencies between 0.1 and 5Hz.

Statistical Analyses in the Literature

Infinite possibilities in experimental design, populations, and questions exist in biomechanics and motor control research. Similarly, a near-infinite range of statistical testing is possible in this field of research. There is no ideal statistical test for all possible study designs, so researchers must dutifully select appropriate testing for their questions based on the strengths and weaknesses of each test and previous literature. A majority of LAE research has employed two-way repeated measures analyses of variance (RANOVAs) in order to compare LAE from different conditions over different time periods. Lee et al., in 2017, utilized two-way repeated measures ANOVAs in order to compare maximal forward lean between two conditions over multiple time periods [30]. Similarly, Kluzik, Peterka and Horak used two-way RANOVAs to compare various incline angles (conditions) and their effects on forward lean across multiple time periods [26]. The same investigation used a two-way repeated measures MANOVA to compare both trunk and ankle angles in a similar fashion after log-transforming each [26]. Wright et al. also used two-way repeated measures

ANOVAs in order compare between several conditions and within two time-quartiles [206].

Summary

Research which utilizes postural adaptation paradigms such as incline-interventions are a useful tool in the study of multisensory integration. Much has been learned from previous research that may be used by clinicians to develop protocols for decreasing fall incidence in at-risk populations. While much has been learned, there remain many questions. Lean after-effect research had yet to address how an additional proprioceptive intervention may alter outcomes. Wright used two proprioceptive interventions and found evidence of sensory reweighting in LAE, while we used tendon vibration, which not only decreases reliability but also induces movement[206]. We know that vibration-induced movements involve the PPC, and that the PPC is involved in multisensory integration [174,178,230]. As such, neuromodulation of the PPC can lead to greater understanding of the neurological processes involved in postural adaptation. This review of the literature highlights the importance of these lines of research and provides a historical perspective for LAE research. This project aimed to further both of these lines of research.

Effects of Shank Vibration on Lean After-Effect

Abstract

The ability to adapt one's posture is an important factor in avoiding falls when faced with changes in the environment. Postural adaptation occurs through alterations in sensory feedback and/or environmental contexts. There is evidence that one's adaptability is related to their ability to sensory information from their sensory systems into one coherent internal representation of their place within the world, as well as their ability to reweight the influence of specific sensory signals in proportion to that signal's reliability. Incline-interventions lead to lean after-effect (LAE), but it is not fully known how sensory reweighting of unreliable signals may affect the formation of LAE or recalibration back to upright with respect to gravity. We tasked a sample of fifteen healthy, young subjects, with performing incline-interventions under normal or conditions designed to decrease proprioceptive reliability either during the intervention or during the after-effect period. We found that tendon vibration during an incline-intervention does not inhibit LAE, but tendon vibration following an incline-intervention can immediately extinguish LAE. These results suggest that decreased proprioceptive reliability does not decrease initial adaptation to an incline-intervention. The results of this investigation improve our understanding of the role of sensory reweighting and sensory integration into postural adaptability.

Introduction

Postural adaptation involves utilization of vestibular, visual, and somatosensory feedback to update the body schema [21,40]. Adaptation of the body schema can be achieved through persistent alteration of sensory feedback or task demands [29]. These adaptations represent updates of the preferred reference point which the postural control system strives to maintain. A change in behavior once sensory feedback or task demands return to normal is called an after-effect, and can be used to infer adaptation of the body schema [19,31]. After-effects dissipate over the course of seconds to minutes [25,31].

Multiple techniques have been developed to study the adaptation of the body schema through alterations of task conditions or feedback [31,232]. One way to induce postural adaptation is through an incline-intervention, a bout of stance which occurs on an inclined surface. These interventions have been found to induce a postural after-effect known as lean after-effect (LAE). After an incline-intervention, there is a global change in the body schema and an alteration of the relationship between preferred orientation and gravitational vertical [26,31]. There is evidence that lean after-effect is dependent on the signal characteristics of the vestibular, visual, and somatosensory systems [27,128,206]. Chong et al. showed that healthy individuals differ in response to those with vestibular loss [205]. Earhart et al. systematically altered the presence of visual feedback during LAE. Whenever visual feedback was provided, LAE was immediately extinguished, but when visual feedback was removed, the subjects began to lean forward again [128]. Wright et al. utilized a sway-referenced platform during LAE to decrease proprioceptive reliability, which lead to faster abolishment of the LAE illusion [206]. Mechanical vibration of the shank, which can occur on the Achilles tendon (ATV) or tibialis anterior (TAV) among other sites, has also been shown to induce shifts in body position as well as after-effects [25]. This investigation sought to expand the understanding of vibration-induced postural adaptation by performing vibration during stance on flat, inclined, and post-inclined surfaces. Furthermore, this investigation sought to identify the effects of tendon vibration on lean after-effect when performed during an incline-intervention to improve our understanding of how support surface characteristics can affect vibration-induced postural illusions. Last, this investigation sought to identify the effects of tendon vibration following an incline-intervention on the extinguishment of LAE.

Methods

Subjects. Fifteen subjects were recruited to perform several postural control tasks across multiple data collection sessions. All subjects provided informed consent through a process in accordance with the Helsinki Declaration which was approved by the University of Houston's institutional review board for experimental studies. Subjects were screened to exclude those who were not between 18-35 years of age, or who had a history of neurological or musculoskeletal dysfunctions that may inhibit postural control or sensory feedback.

Protocol. Subjects performed several postural control tasks. Throughout all trials of each task, subjects were instructed to keep their eyes closed and place their arms on their chest. Subjects were also instructed to, "Stand naturally and not to resist any pulls they felt on their body or temptation to lean," and to, "not pay attention to their posture and let their mind wander." During the first data collection, subjects performed a baseline trial of 30s of quiet stance, as well as trials of ATV and TAV while standing on a flat surface (VB115, Technoconcept, France). For both ATV and TAV, bilateral vibration was applied for 30s, which was immediately followed by 30s of quiet stance (QS). These data are represented in Figure 11.

Next, subjects performed five conditions of incline-intervention. Conditions were administered in a random order and separated by a minimum of 30-minute washout period. Subjects performed at most three conditions per session, leading to a minimum of two sessions per subject to complete the study (Figure 10). Additionally, after the washout period and prior to the start of each protocol, a bout of quiet stance was performed to verify that LAE had completely decayed. For each condition, subjects first performed a 30s baseline trial of QS (T1). Next, they moved atop an inclined surface and stood for five minutes (T2). Last, they moved back to a horizontal configuration and stood for another five minutes (T3). The five conditions of incline-intervention are reported in Table 1.

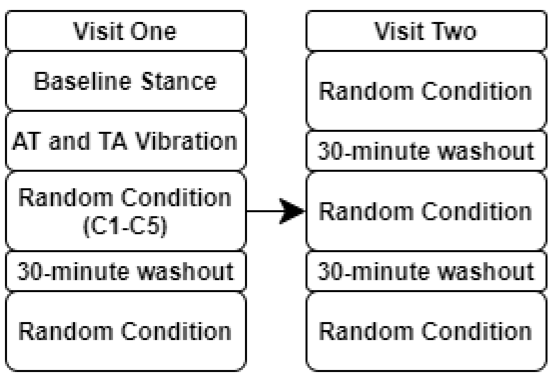

Figure 10. Experimental paradigm. Five experimental conditions were administered over the course of two data collection sessions separated by a minimum of 48 hours.

Table 1. Experimental Conditions

Condition	Parameters
1	No Vibration
2	ATV During T2

3	TAV During T2
4	ATV During T3
5	TAV During T3

Instrumentation. Subjects were measured and outfitted with reflective markers based on the Vicon Plug-in Gait model (Vicon; Oxford Metrics Ltd, Oxford, England). Subjects also wore earmuffs to minimize auditory feedback. Incline-interventions took place on a surface set to an incline angle of 10-degrees (ASAHI Corporation, Gifu, Japan). Tape was laid down in order to aid the subject in returning to the same place after the incline-intervention. Throughout the experiment, motion was captured using a 12-camera Vicon Nexus system at a frequency of 100Hz (Vicon; Oxford Metrics Ltd, Oxford, England). During trials where vibration was present, vibration occurred at a frequency of 80Hz and an amplitude of 1mm (VB115, Technoconcept, France).

Data Processing. Kinematic data were collected and exported from Vicon Nexus 1.8.5. These data were imported and analyzed using custom MATLAB scripts (MathWorks, Inc. Natick, MA). Marker trajectories were utilized to compute a center of gravity (COG) measure which was filtered using a 4th order Low-Pass Butterworth filter with a cut-off frequency of 0.1Hz. This filter design was previously employed to isolate changes in elected positioning while eliminating higher-frequency components of sway [31]. Center of gravity was also band-pass filtered between 0.1 and 5Hz in order to calculate path length in the anterior-posterior direction (AP-Path Length) to serve as a measure of postural sway. The effects of vibration were quantified by measuring sway before, during, and after vibration as well as the change in position during those time periods.

Low-Pass filtered kinematic data acquired during T3 for each condition were utilized to calculate two measures which quantified LAE. Off-Set Time identified when the subject ceased leaning forward, and was defined as the first moment in time, following the peak anterior position, in which the subject returned to an average position within 2SD of their baseline for a period of 10s. Next, Integrated Area was calculated using measures adapted from previous studies. While the previous studies summed area under a positional curve until subjects reached the Off-Set Time, we summed the area under the curve throughout the entire 300s trial. This was performed because a many of T3 trials did not exhibit obvious decay over time, and subjects often briefly returned to upright before starting to lean again [31]. Integrated Area was identified as the mathematical summation of the data throughout all points during which the subject was greater than 2SD anterior to their baseline value throughout the trial.

Statistical Analysis. In order to identify the basic effects of vibration, separate one-way Repeated Measures Analysis of Variance (RANOVA) were used to compare average COG position before, during, and after vibration for ATV and TAV during flat stance. Next, in order to compare whether there was a difference in the shift of COG position brought on by ATV when performed either an inclined or flat surface, a Two-Way (Position prior to and during vibration by surface configuration) RANOVA was performed. This process was repeated comparing TAV on a flat and inclined surface, as well as ATV and TAV on a flat surface and post-inclined stance.

Differences in postural sway were identified by comparing AP-Path length between no vibration, ATV, and TAV conditions using a One-way RANOVA. This analysis was performed for flat, inclined, and post-inclined stance.

In order to identify whether there was an effect of vibration during inclined stance on the formation of LAE, separate One-way RANOVAs were used to compare Off-Set Time and Integrated Area between C1-C3. Then, in order to identify the whether there was an effect of vibration during T3 on the re-calibration back to upright (i.e. the extinguishment of LAE), separate One-way RANOVAs were used to compare Off-Set Time and Integrated Area between C1, C4, & C5. All statistical analyses were carried out using SPSS (IBM, Chicago, IL). In the case of significant findings, pairwise comparisons were made using a Bonferroni post-hoc adjustment. In the case of violated assumptions of sphericity, a Greenhouse-Geisser correction was employed. Effect sizes, derived from partial eta squared (n_2), were also derived in cases of significant findings. When significant pairwise comparisons were identified, Hedge's G (HG) effect sizes were calculated. For all analyses, significance was identified using an alpha value of $p<0.05$.

Results

Subjects. Fifteen subjects (f=9) participated in this series of experiments. Subjects ranged from 19-30 years old (23.5±3.7), had an average height of 167±13.5cm, and weight of 77.6±21.1kg. For the bouts of vibration which occurred independent of any incline-intervention, ATV led to significant changes in position throughout the trial ($F_{2,13}=163$ $p<0.0001$, $n_2=0.96$) (Fig 11). Post-hoc comparisons using a Bonferroni adjustment revealed a significant posterior shift during vibration (p<0.0001 HG=2.07) and an anterior after-effect following vibration (p<0.0001 HG=2.08). TAV also led to significant changes in position ($F_{2,13}$=16.3 p<0.0001, n_2 =0.77) overall, with a significant anterior shift during vibration (p<0.0001 HG=1.24) but no after-effect (p=0.31).

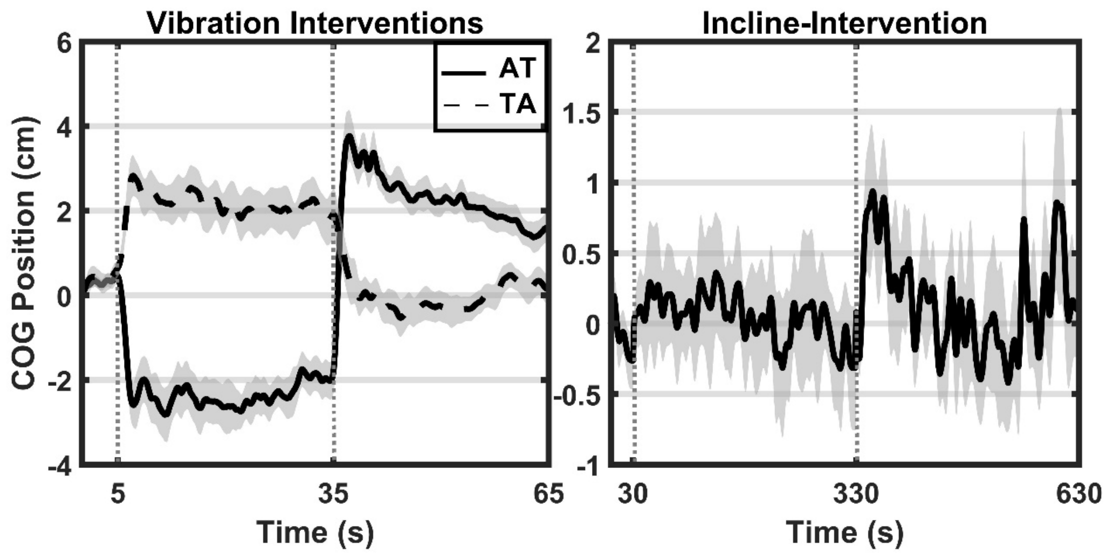

Fig 11. Left: Mean COG displacement (±1SEM) of responses to AT and TA vibration occurring independent of inclined stance. First and second horizontal bars represent onset and off-set of vibration, respectively. Right: Response to C1 incline-intervention without any concurrent vibration intervention. First and second horizontal bars represent onset of T2 and T3, respectively [233]

Unlike the typical response to TAV, when TAV occurred on an inclined surface (i.e. during T2 of the incline-intervention), there was no anterior shift ($F_{2,13}$=7.4 p=0.007, n_2=.53). Specifically, when applied on a flat surface, TAV led to an anterior shift of 2.14±1.8cm. When applied on an inclined surface however, TAV led to a slight posterior shift in position of -.73±2.05cm, differing significantly from flat response (p=0.0003 HG=1.48). Conversely, ATV led to a posterior shift in COG of similar magnitude when performed either on a flat or inclined surface ($F_{2,13}$=0.79 p=0.47) (Fig 12).

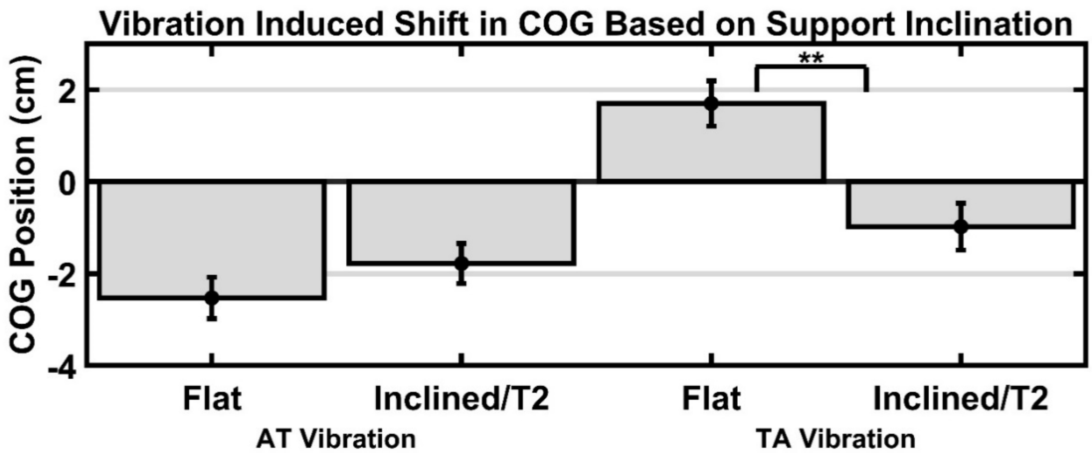

Fig 12. Mean change in AP-COG position upon the onset of vibration on a flat surface compared to during inclined stance (±1SEM) Asterisks (**) indicate statistical significance with corresponding p value <0.005

When presented on a flat surface, ATV led to a posterior shift of -2.54±1.68cm. This posterior shift was significantly reduced when ATV occurred post-incline (i.e. during T3 of the incline-intervention) ($F_{2,13}$=7.39 p=0.018, n_2=0.36). During T3, a shift of only -1.03±2.05 was found. No such differences were found when comparing the typical response to TAV with response to TAV during post-inclined stance ($F_{2,13}$=0.4 p=0.84) (Fig 13).

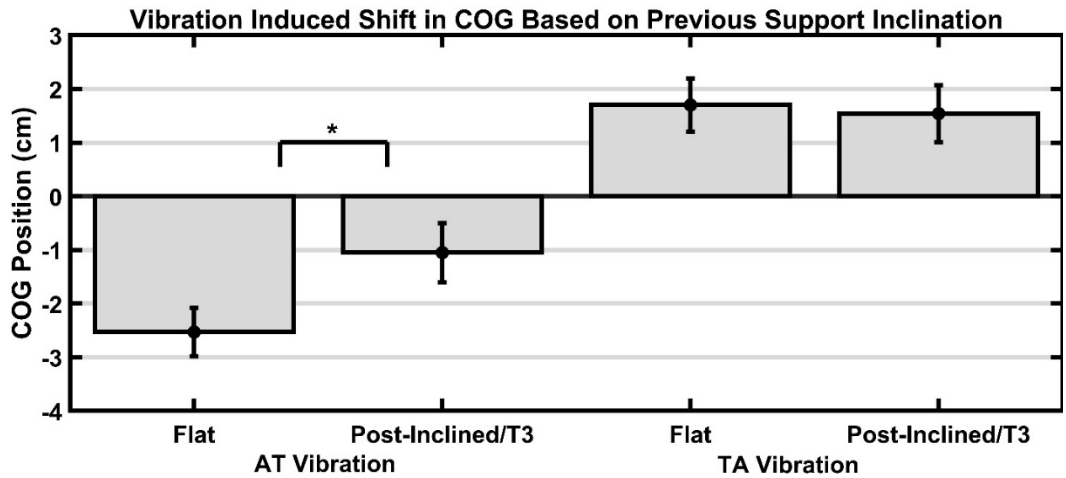

Fig 13. Mean COG position following vibration on flat compared to when performed following inclined stance (±1SEM) Asterisks (*) indicate statistical significance with corresponding p value <0.05

Both ATV and TAV during flat stance led to increased postural sway, as measured by AP-Path Length compared to quiet stance ($F_{2,13}$=19.3 p<0.0001, n_2=0.73; ATV p<0.0001 HG=1.48; TAV p<0.0001 HG=1.58). Vibration during inclined stance (i.e. T2) also led to increased postural sway compared inclined stance without vibration ($F_{2,13}$=42 p<0.0001 n_2=0.87; ATV p<0.0001 HG=1.62; TAV p=0.012 HG=1.35). Conversely, vibration during post-inclined (T3) stance led to no increase in postural sway compared to post-inclined stance with no vibration ($F_{2,13}$=1.38 p=0.06) (Fig 14).

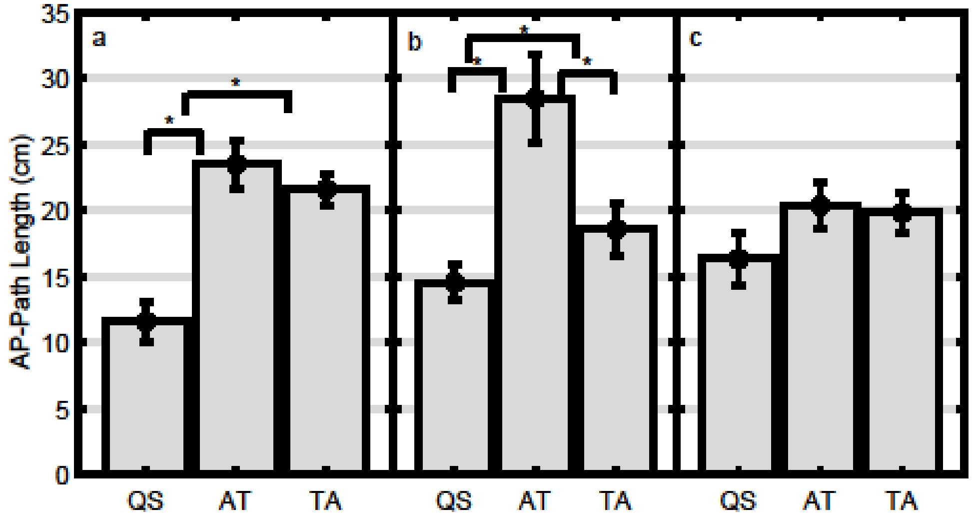

Fig 14. Mean path length in anterior-posterior direction (±1SEM) a- on a flat surface b- on an inclined surface c- following inclined stance Asterisks (*) indicate statistical significance with corresponding p value <0.05

There were no differences in the magnitude or duration of LAE between C1-C3 (i.e. no-vibration, ATV during T2 and TAV during T2) (Fig 15). No differences were observed in Off-Set Time, indicating the time to calibrate to gravity was not affected (($F_{2,13}$=0.42 p=0.67). There were also no differences in the measurement of Integrated Area, indicating that the magnitude of LAE was not affected ($F_{2,13}$=0.46 p=0.64).

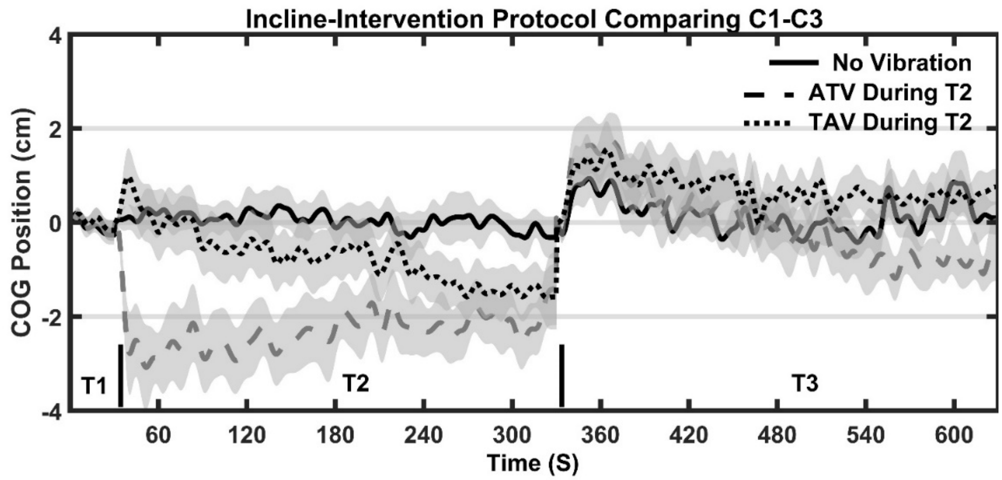

Fig 15 Mean COG displacement (±1SEM) throughout the incline-intervention protocol comparing C1-C3. T2 started at 30s and T3 started at 330s (5 minutes and 30 seconds).

When vibration was presented during T3 (C4 & C5), however, significant changes were observed in Off-Set Time ($F_{2,13}$=9.79 p=0.003 n_2=0.60) (Fig 16). TAV during T3 led to a significantly longer Off-Set Time than the no vibration or AT conditions (p=0.009 HG=0.66, p=0.002 HG=1.15, respectively). There was no difference between the ATV and no vibration condition (p=0.85). Similarly, there were significant differences between conditions in Integrated Area $F_{2,13}$=9.26 p=0.003 n_2=0.59) TAV during T3 led to significantly greater Integrated Area than ATV (p=0.002 HG=1.3).

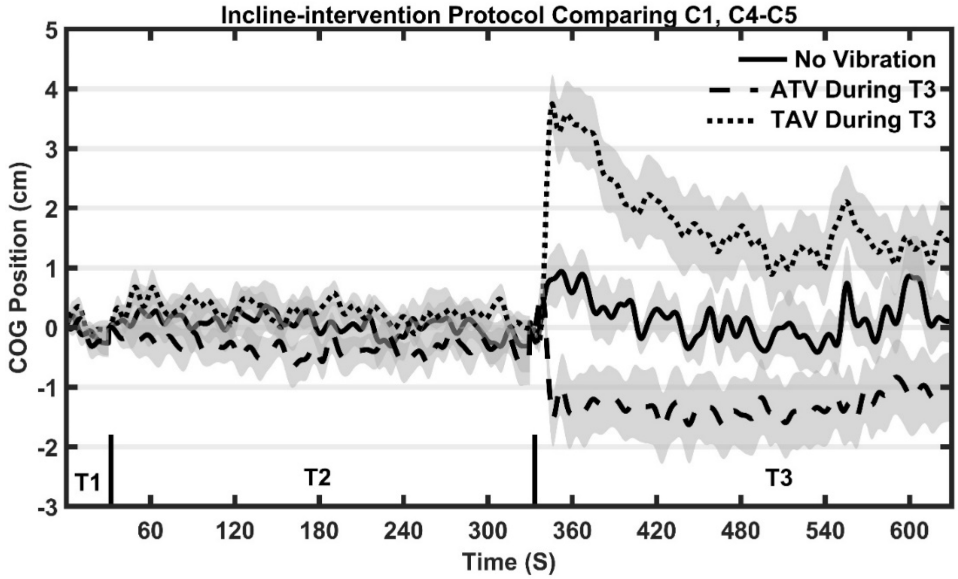

Fig 16 Mean COG displacement (±1SEM) throughout the incline-intervention protocol comparing C1, C4, and C5 T2 started at 30s and T3 started at 330s (5 minutes and 30 seconds).

Discussion

Vibration-induced shifts in COG are dependent on support surface characteristics. On a flat surface, TA vibration induced an anterior shift. Conversely, on an inclined surface, TA vibration induced a slight posterior shift. There are at least two reasonable explanations for this phenomenon. First, postural instability decreases the effects of tendon vibration on position via proprioceptive downweighting [234]. In the current study, sway was increased during inclined-stance compared to flat stance, which could decrease the effects of tendon vibration. The fact that only the effects of TAV, and not ATV were muted suggests that this is unlikely to be the case. Furthermore, if proprioceptive downweighting had occurred, we would have likely observed differences in LAE between the conditions (C1-C3) [27,206].

Another possible explanation for this effect would be limiting biomechanical factors. The lack of anterior shift during inclined stance may be due to the increased ankle dorsiflexion inherent to inclined stance. If subjects increased their dorsiflexion to an even greater extent in response to TA vibration, the additional dorsiflexion may have exceeded the subject's base of support. Instead, subjects may have used an orientation closer to gravitational vertical in order to maintain stability. These constraints were not present in ATV, which leads to more dorsiflexion, explaining why response to ATV was not affected. This explanation is coherent with the lack of differences in LAE between the three conditions.

Following an incline-intervention (i.e. during T3), the posterior shift associated with ATV was decreased. These findings show that the anterior shift which results from an incline-intervention (i.e. LAE) can alter typical responses to vibration. This may suggest some sort of summative effect between the anterior LAE and the posterior shift from ATV. Previous investigations have shown summative effects during two concurrently presented interventions [120]. Kabbaligere et al. found that when presented individually, ATV lead to a posterior shift and the visual perturbation they employed led to an anterior shift. When presented together however, the response was close to a mathematical summation of the two perturbations suggesting a summative or middle ground response [120]. To the best of our knowledge, this is the first investigation to show a summative effect of two interventions on postural adaptation that both affect the proprioceptive channel.

Stability decrease associated with tendon vibration depends on context. Support surface characteristics were related to the increase in postural sway, measured by AP-Path Length, associated with tendon vibration. For both flat and inclined stance, both AT and TA vibration increased sway compared to non-vibrated stance. No such differences were found during T3. Previous studies have found that unstable support surfaces such as foam or a Bosu ball decrease the stability loss associated with vibration [235,236]. While T3 stance occurred on a stable surface, there was an increase in instability compared to baseline associated with this period, even when vibration was not present. The lack of significant stability decrease between the post-inclined conditions may be partially explained by increased 'baseline' sway during T3 compared to regular quiet stance. Nevertheless, the *cost* of vibration on postural sway decreased when preceded by an incline-intervention. There is evidence that higher levels of variability, namely during reaching tasks, can improve motor learning [237,238]. It is possible that increased adaptive challenge during the incline-intervention was utilized in order to lead to improve the subject's ability to maintain a stable posture during the post-incline period, regardless of the presence of vibration.

Vibration during inclined stance did not influence lean after-effect No differences were found between conditions for either measure of LAE between C1-C3. Multiple previous studies have identified a positive relationship between proprioceptive weighting and the strength of LAE [128,205,206]. In one experiment, Chong et al., increased LAE response in some subjects by adding augmented light touch feedback during the incline-intervention. They argued that providing this feedback increased the weight placed on the somatosensory system in their population, leading to greater LAE. Conversely, in our study, disrupting proprioceptive feedback via tendon vibration during an incline-intervention (i.e. T2) did not affect LAE. These results suggest that LAE is not affected by induced downweighting of the proprioceptive system, which stands in contrast to several previous arguments [31,128,205,206]. These differences may be explained by multiple factors. First, some of these studies have induced proprioceptive downweighting post-incline intervention (i.e. T3), not during the incline-intervention (T2) [128,206]. These do not necessarily show the impact of sensory weighting on the development of LAE, but rather on the extinguishment of LAE. Additionally, the light-touch feedback provided by Chong et al. occurred through a different channel (haptic versus proprioceptive) and on a different body segment (finger versus shank). The current study may have found no difference in LAE because unlike the previous studies, we performed two concurrent interventions of the same proprioceptive channel on the same segment, which could be more direct method of identifying the role of proprioceptive weighting on the formation of LAE

Vibration during T3 significantly altered LAE. Results of comparisons between C1, C4, and C5 demonstrate that LAE can be altered by tendon vibration. Previously, Wright found that sway-referencing the COP following an incline-intervention quickly led to abolishment of LAE and a return to gravitational vertical [206]. Wright argued that this was due to downweighting of the proprioceptive system, which is a well-founded argument [107,205]. Despite the decreased proprioceptive reliability associated with tendon vibration, we did not observe a general decrease in LAE following vibration. Instead, we found direction-specific modifications in LAE depending on whether the AT or TA was vibrated. This suggests that the effects of vibration on position dominated the relative downweighting of the proprioceptive system. The direction specific effects of vibration suggest there is a summative adaptation which occurs when vibration is performed post-inclined stance. Previous research has found concurrent adaptations [25,54,120,239]. To the best of our knowledge, this is the first investigation to find a summative effect of two interventions which occur subsequently (i.e. performing an incline-intervention to form lean after-effect and subsequently performing tendon vibration).

Conclusions. We found evidence that altering support surface characteristics impacts the effects of tendon vibration on position. We also found that tendon vibration during inclined stance does not affect the formulation of LAE. Alternatively, tendon vibration during LAE leads to direction-specific responses based on what tendon is vibrated. Last, the increased sway typically observed during vibration is absent during LAE. This information improves our general understanding of sensory integration and reweighting during postural control by expanding our understanding of intrasensory effects of multiple proprioceptive interventions. Results of this investigation may lead to improvements in testing of adaptability in response to multiple perturbations as well as potential improvements in training of adaptability in clinical populations.

Non-invasive brain stimulation of the posterior parietal cortex alters postural adaptation

Abstract

Effective integration of sensory information is required to promote adaptability in response to changes in the environment during postural control. Patients with a lesion in the posterior parietal cortex (PPC) have an impaired ability to form an internal representation of body position, an important factor for postural control and adaptation. Suppression of PPC excitability has also been shown to decrease postural stability in some contexts. As of yet, it is unknown whether stimulation of the PPC may influence postural adaptation. This investigation aimed to identify whether transcranial direct current stimulation (tDCS) of the bilateral PPC could modulate postural adaptation in response to a bipedal incline postural adaptation task. Using young, healthy subjects, we delivered tDCS over bilateral PPC followed by bouts of inclined stance (incline-interventions). Analysis of postural after-effects identified differences between stimulation conditions. Following an incline-intervention, inhibition of either hemisphere of the PPC decreased lean after-effect. Results reinforce the notion that the PPC is involved in motor adaptation and extend this line of research to the realm of standing posture. The results further highlight the role of the bilateral PPC in utilizing sensory feedback to update one's internal representation of verticality and demonstrates the diffuse regions of the brain which are involved in postural control and adaptation. This information improves our understanding of the role of the cortex in postural control, highlighting the potential for the PPC as a target for sensorimotor rehabilitation.

Introduction

Central integration of visual, vestibular, and proprioceptive sensory information is critical for successful postural control and the maintenance of upright stance (Peterka 2002). Another important component of successful postural control is adaptability. Postural adaptation requires the updating of one's internal representation of their position and movement within the environment (Chritchley 1953; Head & Holmes 1911). The internal representation can adapt in response to changes in sensory feedback and/or the external environment. These changes occur slowly and correspond with changes in behavior which gradually reduce movement errors (Gurfinkel et al. 1995). Once original conditions are restored, there is an after-effect while the internal representation recalibrates to its previous state (Ivanenko & Gurfinkel 2018; Kluzik et al. 2005). After-effects dissipate over the course of seconds to minutes as prior experience and sensory feedback reverts the adapted internal representation to baseline (Kluzik et al. 2005; Wierzbicka et al.1998). This investigation sought to improve our general understanding of how the posterior parietal cortex (PPC) is involved in postural adaptation.

Multisensory integration is impaired in individuals with lesions of the (PPC) (Derouesne et al. 1984). This is because the PPC is a sensory association area, where signals from multiple sensory systems (i.e. the visual, vestibular, and somatosensory systems) are integrated [241]. The PPC performs calculations, transforming sensory signals into sensorimotor representations of the body position in order to create an internal representation of our position in space [242–244].

There is some evidence of left hemisphere parietal lobe dominance in motor adaptation. Specifically, Mutha et al. identified that brain damage to the left PPC (lPPC) decreased visuomotor adaptation but damage to the right PPC (rPPC) did not [39]. Newport et al. found that a bilateral lesion of the PPC, primarily in left the hemisphere, led to an inability to adapt to visual perturbations in a pair of 2006 case studies [245,246]. Other investigators have shown that disruptive TMS of the left PPC can impair adaptive reaching during a right-handed task [190]. Alternatively, there is evidence that the right hemisphere parietal lobe, as part of a network with the right inferior frontal cortex, dominates processing of positional illusions induced by tendon vibration [179,247]. Still others have found some level of bilateral activity associated with positional illusions brought on by tendon vibration [178,248].

While the effects of brain stimulation of PPC has yet to be explored regarding postural adaptation, previous research has demonstrated the PPC's involvement during postural control tasks with additional sensory integration demands (Ishigaki et al. 2016; Kaulmann et al. 2017). Both Kaulmann et al. and Ishigaki et al. identified that inhibition of the PPC via non-invasive brain stimulation altered the effects of augmented sensory feedback on postural stability. Based on the fact that the PPC is involved in upper body motor adaptation, processing of proprioceptive perturbations, and sensory integration during postural control, it is reasonable to hypothesize that the PPC is also involved in postural adaptation. It is yet unclear what hemisphere may dominate in the task of postural adaptation. There is evidence that the bilateral PPC is involved in continuous postural control during periods of sensory conflict [250]. Furthermore, a previous investigation by Heinen et al. identified that bilateral stimulation of the PPC was more effective at eliciting changes in working memory than unilateral stimulation. Thus, bilateral roles of the PPC should be investigated within the scope of postural adaptation. It is important to understand if there are hemisphere-specific roles of the PPC in postural adaptation or if the involvement is part of a more diffuse cortical network which requires bilateral PPC input.

To identify if relative facilitation or inhibition of the PPC alters postural adaptation, we employed bilateral transcranial direct current stimulation (tDCS). tDCS provides low intensity stimulation, flowing from anodal to cathodal electrode(s), which results in slight alterations in the excitability of underlying cortical tissue (Lefaucheur & Wendling 2019). Anodal stimulation leads to a relative excitation of the underlying tissue while cathodal stimulation leads to a relative depression. Sham stimulation does not alter cortical excitability (Lefaucheur & Wendling 2019). While there is no consensus, some previous investigations have found behavioral differences between sham and cathodal, but not sham and anodal stimulation [252,253]. Improving the understanding of the PPC's role in postural adaptation will improve the basic understanding of cortical influences on postural control and may have clinical implications for use of non-invasive brain stimulation to improve adaptability in fall-risk populations.

To identify differences in postural adaptation resulting from tDCS of the PPC, this investigation utilized an incline-intervention adaptation paradigm. Incline-interventions involve prolonged stance on an inclined surface and result in a postural after-effect known as lean after-effect (LAE), which is an anterior shift in position that can persist for several minutes (Chong et al. 2017; Chong et al. 2014; Kluzik et al.

2005). Lean after-effect reflects a change in the internal relationship between gravitational vertical and elected postural orientation. This incongruence is corrected over time as subjects reorient to gravity [31]. The current investigation sought to determine the effects of bilateral tDCS stimulation of the PPC on adaptation to the inclined surface, as well as on de-adaptation once conditions return to normal.

Table 1. Definitions

CENTER OF GRAVIY	COG	Approximation of one's overall position in space
LEAN AFTER-EFFECT	LAE	Postural after-effect indicating adaptation, specifically adaptation to an incline-intervention
POSTERIOR PARIETAL CORTEX	PPC	Hub of multisensory integration in the cortex
TRANSCRANIAL DIRECT CURRENT STIMULATION	tDCS	Leads to depolarization or hyperpolarization of local brain tissue based on stimulation condition
CATHODAL	RC or LC	Leads to relative hyperpolarization
ANODAL	RA or LA	Leads to relative depolarization
SHAM	Sham	Placebo

Methods

Subjects. Fifteen subjects were recruited to perform postural control tasks after tDCS stimulation across three data collection sessions. An additional fifteen subjects participated in a control experiment. All subjects provided their written informed consent in accordance with the Helsinki Declaration. Consenting documents were approved by the University of Houston institutional review board for experimental studies. Inclusion criteria included subjects being between 18-35 years of age, no history of neurological or musculoskeletal dysfunction that may inhibit postural control or sensory feedback, and no known contraindications to tDCS stimulation such as metallic implants, history of seizures or brain damage (Datta et al. 2011).

Protocol. Subjects participated in three sessions, which were separated by a minimum of 48 hours. During each session, subjects performed an incline-intervention, which consisted of three trials (Fig 17). First, subjects performed a 30s baseline trial of quiet stance (T1) on a horizontal surface. Next, they moved atop an inclined surface set to an angle of ten degrees for five minutes (T2). Last, subjects returned to standing on the horizontal surface (T3) where they stood for a final five minutes (Fig 1). Throughout the task, subjects were instructed to keep their eyes closed, place their arms across their chest, and stand naturally without, "resisting any pulls they felt on their body or temptation to lean." Transcranial direct current stimulation was applied at the beginning of each session and was administered in a random order. Stimulation was administered in three conditions: Right Anodal-Left Cathodal (RA-LC), Right Cathodal-Left Anodal (RC-LA) and Sham. For all conditions, stimulation was initiated prior to the incline-intervention (i.e. before T1). For the first 15 minutes of stimulation, the subject sat quietly, then, at the 15-minute mark, subjects began to perform the protocol. First, subjects performed the baseline trial (T1), then moved atop the inclined surface for T2, then immediately began T3. Stimulation was terminated at the end of T2. Stimulation order was double-blinded to the subject and the administrator of the experiment.

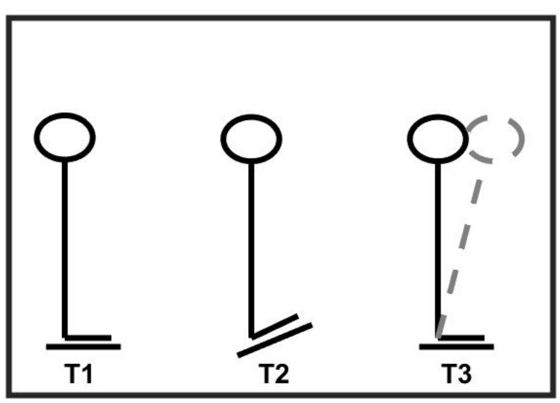

Fig 17: Representation of T1 (baseline) T2 (incline-intervention) and T3 (lean after-effect period).

Instrumentation. Incline-interventions were performed on a surface set to an incline angle of 10-degrees (ASAHI Corporation, Gifu, Japan). Kinematic experimental data were collected using a 12-Camera Vicon motion capture system. Subjects were measured and outfitted with reflective markers based on Vicon Nexus's Full Body Plug in Gait Marker Set (Vicon, Oxford, UK). Kinematic data from all trials were captured at a rate of 100Hz. Subjects also wore earmuffs to minimize auditory feedback. tDCS stimulation was performed using an eight-channel Starstim tDCS Device (Neuroelectrics, Spain). Saline soaked 25cm^2 sponges were placed at P3 and P4 using the international 10-20 system [255]. Two active stimulation conditions were used, right hemisphere anodal left hemisphere-cathodal (RA-LC), and right cathodal-left anodal (RC-LA). The third condition was a Sham condition, where current was ramped up over the course of 30s and ramped down after 30s of stimulation in order to simulate the scalp sensation of active stimulation without altering cortical excitability. For both active conditions, stimulation was applied at 1.5mA.

Data Processing. Kinematic data collected during the experiment were exported from Vicon Nexus and analyzed using custom MATLAB scripts (Mathworks, Inc, Natick, MA). Marker trajectories of the legs and torso were utilized to compute the anterior-posterior center of gravity (COG) measurement. Based on previous literature, data derived from incline-interventions was filtered using a 4th order low-pass Butterworth filter with a cut-off frequency of 0.1Hz. This design can isolate changes in mean center of gravity while eliminating signal higher frequency COG fluctuations during prolonged trials (Kluzik et al. 2005).

T3 AP-COG measures were baseline corrected to reflect pre-adaptation position. Thus, any anterior measure of COG is relative to pre-adaptation stance, not absolute position. Because tDCS started before and continued throughout the baseline trial (T1), it may have altered the characteristics of baseline stance in a stimulation-specific manner thus confounding our baseline corrected T3 AP-COG measure. Therefore, we ran a control experiment where fifteen additional participants experienced the incline-intervention (i.e. T1, T2, and T3) without receiving tDCS. We compared mean position, standard deviation of position, as well as path length between stimulation conditions and the control condition (unstimulated). The COG data derived from baseline corrected post-inclined stance (T3) was used to calculate several outcome measures reflecting the magnitude of postural adaptation (LAE). Before any further calculations, two time periods were identified, the first 30s of T3 was defined as the Early LAE period while the final 30s was defined as the Late LAE period. The Max LAE was also calculated, which was defined as the maximum anterior AP-COG during the Early LAE period. As subjects were readapting after the incline intervention, the COG gradually returned to vertical. Therefore, the Max LAE always occurred in the Early LAE period. Average AP-COG (Ave-COG) during the Early and Late periods of T3 were also calculated in order to identify the magnitude of LAE present during each time period. Finally, Off-Set Time, the first sample following Max LAE in which the subject returned to an average position within two standard deviations (SD) of their baseline position for a period of 10s was calculated in order to identify what, if any, effect stimulation condition had on the time-course of recalibration to upright stance (Kluzik et al. 2005; Kluzik et al. 2007).

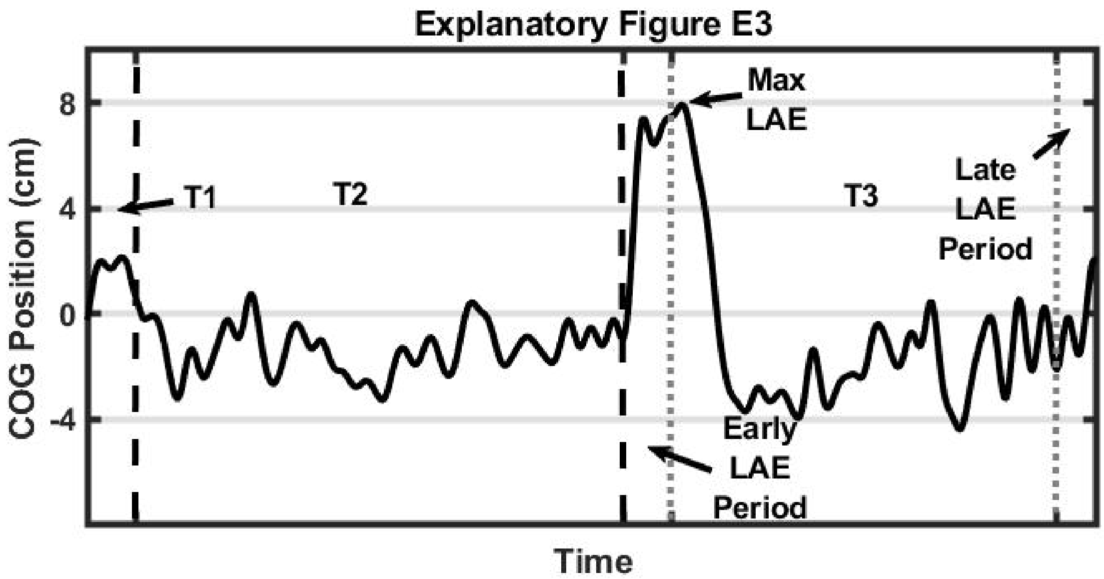

Fig 18. Graphical representation of data processing parameters. Black dotted lines indicated transitions between trials. Grey dashed lines indicate measurement periods. Data is from one representative trial.

Statistical Analysis. To verify that tDCS did not alter baseline stance, average position in the AP direction, standard deviation of AP position, AP-path length, and root mean square (RMS) of AP position were compared between stimulation conditions during T1. An additional sample of baseline measures from fifteen subjects who did not receive tDCS stimulation was also included in the comparison in order to verify that Sham stimulation did not alter unperturbed stance. Comparisons were made using separate repeated measures Analysis of Variance (rm-ANOVA) for each variable. Next, to identify the effects of tDCS stimulation on lean after-effect (LAE), a two-way rm-ANOVA (Time by Position) was performed to compare average AP-

COG during the Early and Late periods of T3 between the stimulation conditions. Follow-up one-way ANOVAs were utilized to compare average AP-COG during Early and Late LAE periods as well as for Max LAE and Off-Set Time between stimulation conditions. Pairwise comparisons for analyses were made using Bonferroni post-hoc adjustments. For all analyses, significant findings were defined by an alpha value of $p<0.05$. Effect sizes, derived from partial eta squared (n_2) for main effects and Hedge's G (HG) for pairwise differences were also derived in cases of significant findings. Statistical analyses were performed using SPSS (Version 25.0. Armonk, NY: IBM Corp.).

Results

Fifteen subjects, eight females and seven males, completed the study. Subjects were aged 23.4±4.2 years, were 165.6±12.6cm tall and weighed 77.4±18.3kg. When asked at the end of each session to identify what stimulation condition they had received, subjects guessed correctly 1.0±0.78 times out of three indicating that subjects were generally unaware of what stimulation condition they were experiencing. Results of one-way rm-ANOVAs revealed no difference between stimulation conditions for mean position ($F_{3,12}=0.59$ $p=0.63$), standard deviation of position ($F_{3,12}=0.24$ $p=0.74$), AP path length ($F_{3,12}=0.14$ $p=0.93$) or RMS of AP position ($F_{3,12}=0.29$ $p=0.83$). This analysis included results from fifteen pilot subjects who received no brain stimulation (i.e. unstimulated), demonstrating that tDCS did not alter the characteristics of stance during the baseline trial T1. These data can be seen in Fig 19.

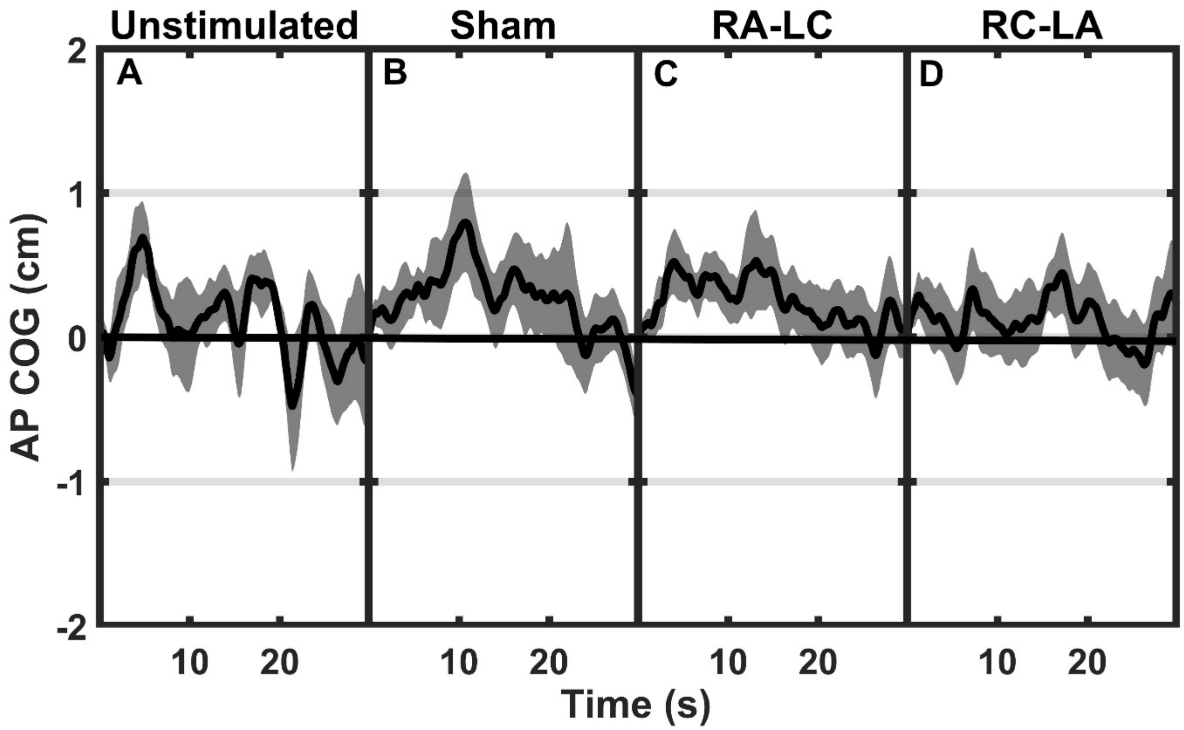

Fig 19. Group Average AP COG±1SEM during baseline (T1) trials. There were no significant differences between simulation condition for measurements of average AP-COG, standard deviation of AP-COG, or path length. The unstimulated (A) chart represents subjects who did not receive any tDCS stimulation [233].

A one-way rm-ANOVA of the maximum AP-COG (Max COG) revealed a main effect of tDCS stimulation ($F_{2,13}$=8.33 p=0.005 n_2=0.356) (Fig 20. Panel A). Post-hoc comparisons found that both active stimulation conditions exhibited significantly less maximum forward lean than Sham (RA-LC p=0.009 HG=0.61; RC-LA p=0.03 HG=0.42), but there was no difference between the two-active stimulation conditions. Analysis of COG data derived from the lean after-effect period revealed that tDCS stimulation altered responses to inclined stance. This is shown by differences in lean after-effect during T3 (Fig 20). Results of a two-way rm-ANOVA comparing Ave-COG during Early and Late LAE periods between stimulation conditions revealed a significant overall effect of condition and a significant effect of time (Condition- $F_{2,13=}$7.61 p=0.006 n_2=0.54, Time- $F_{1,14}$=5.2 p=0.039, n_2=0.27,). However, there was no interaction effect between time and condition ($F_{2,13}$=.36 p=0.27). Additional analyses identified a significant main effect of stimulation conditions for Ave-COG during Early LAE ($F_{2,13=}$3.93 p=0.046 n_2=0.38), but pairwise comparisons using Bonferroni post-hoc adjustments revealed no specific differences between stimulation conditions (Sham to RA-LC p=0.07, Sham to RC-LA p=0.14 , RA-LC to RC-LA p=1) (Fib 20. Panel B). Condition also influenced the Ave-COG during the Late LAE period ($F_{2,13=}$8.47 p=0.004 n_2=0.57). Subsequent pairwise comparisons revealed that the RA-LC and RC-LA conditions each exhibited significantly less Ave-COG during Late LAE compared to the Sham condition (p=0.008, HG=0.94; p=0.003, HG=0.98 respectively). In fact, the Ave-COG in the Late LAE for both active stimulation conditions were posterior to baseline (Fig 20. Panel C). Again, average COG during the Late LAE period was no different between active conditions. There were no differences in Off-Set Time between the three stimulation conditions (p=0.397).

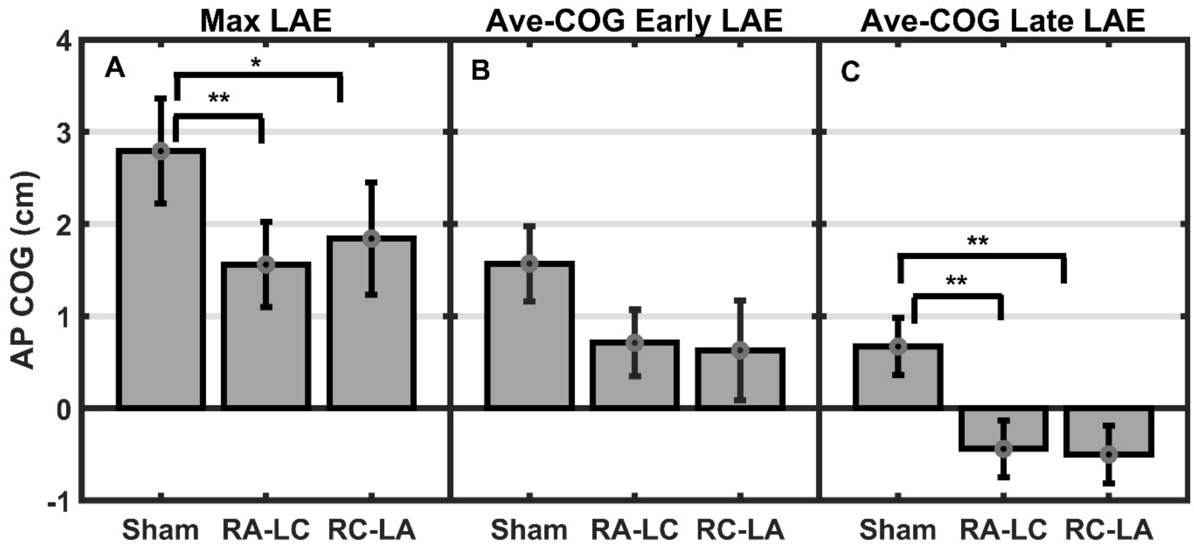

Fig 20. Active stimulation significantly altered Max LAE (A) and Ave-COG during Early (B) and Late (C) periods. Pairwise comparisons show that both active stimulation conditions significantly decreased Max LAE compared to Sham and resulted in COG during the Late LAE period than Sham. Error bars represent±1SEM.

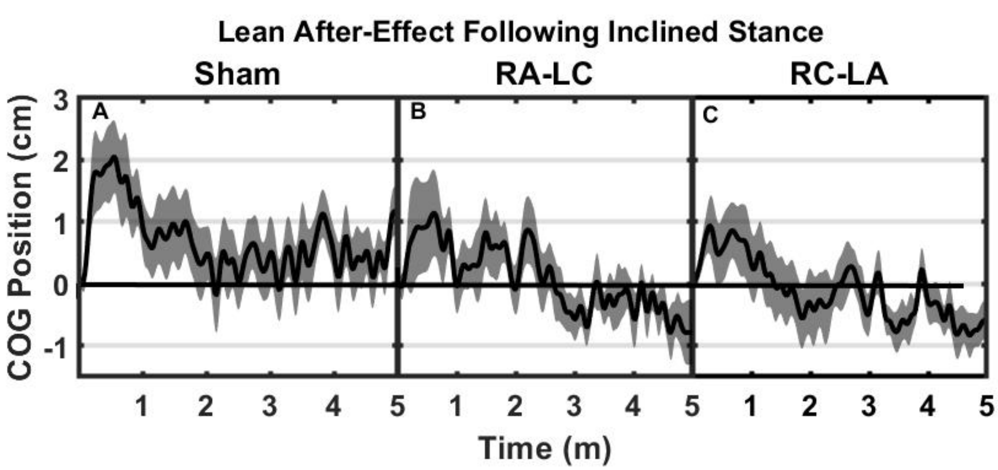

Fig 21. Mean±1SEM of AP COG position during T3 after Sham (A), RA-LC (B) and RC-LA (C) stimulation.

Discussion

The current investigation was designed to assess the role of the PPC in postural adaptation within a group of fifteen healthy, young adults. Neuromodulation was applied in three conditions: RA-LC, RC-LA, and Sham and in a random, double-blind fashion. Postural adaptation, measured by lean after-effect, was decreased in both active stimulation conditions compared to Sham. These findings demonstrate that active stimulation decreased initial adaptation to the incline-intervention (i.e. less forward lean). Furthermore, a significant effect of time showed that LAE significantly decreased throughout the five-minute after-effect period. Off-Set Time was not different between conditions, which shows that while the magnitude of the adaptation was affected, the time course necessary to re-orient to gravity was not. These findings suggest impaired adaptability of the internal representation of one's body position following active stimulation of the PPC, regardless of which hemisphere was inhibited and which was excited.

Evidence indicates that PPC integrates sensory information from the visual, vestibular, and proprioceptive systems in order to maintain an internal representation of one's posture, which is continuously updated to influence motor commands [38,103]. During this experiment, we observed no difference in LAE between active stimulation conditions (i.e. RA-LC and RC-LA). This finding is of interest, because there are some experiments which have sought to identify hemisphere-specific roles of the PPC. Studies have suggested that the right hemisphere may be activated to a greater extent than the left in response to proprioceptive manipulations leading to movement illusions, such as tendon vibration [178,248,256,257]. In a series of studies, Naito et al. identified increased activity in the right inferior parietal lobule (IPL) during tendon vibration, which they identify as part of a frontoparietal network involved in proprioceptive processing to maintain a sense of position [256]. According to the same group, the left IPL may be biased towards computations which associate self-position and the external environment and may be less sensitive to proprioceptive perturbations [178]. Conversely, the left hemisphere PPC has been suggested to be an area closely associated with motor adaptation.

In a pair of case studies, Newport et al. identified impaired prism adaptation in a patient with bilateral damage to the PPC, with greater damage in the left hemisphere [245,246]. Later, these results were clarified by Mutha et al. [39]. In their study, Mutha et al. found that visuomotor adaptation was hindered in subjects with lesions of the left, but not right parietal region. The authors argued that the left parietal region is involved in modifying the internal representation of self-position, and the relationship between movement and the environment [39]. While Mutha et al., suggested that the left parietal region was more important for visuomotor adaptation, the current investigation found decreased postural adaptation through inhibition of either hemisphere. There are several possible reasons for these findings.

For many visuomotor adaptation experiments, a unilateral upper limb task has been employed, which could induce greater activation in the contralateral hemisphere than a bilateral task. Simply by the nature of postural control as a bilateral task, there may be increased bilateral input from a number of cortical areas. Postural adaptation tasks also include stability demands, unlike upper body adaptation tasks. Sensory processing may be altered by additional stability related requirements including the updating of the internal representation of the body and its relationship to gravitational space. Previous investigations have found increased PPC activation during difficult postural control tasks when exposed to multiple sensory perturbations [129]. Unfortunately, Takakrua et al. were only able to record hemodynamics from the right hemisphere and were unable to identify if bilateral increases in activity were present. In healthy subjects, Ishigaki et al. found altered sensory integration of augmented feedback from cathodal tDCS stimulation of the lPPC during postural control, however their study utilized light touch only on the right hand [230].

As the PPC has not previously been studied through the lens of postural adaptation, it was not apparent if there would be hemisphere specific contributions in response to a postural incline task. While the results of the current investigation cannot delineate specific roles of the hemispheres, the results suggest that both hemispheres are involved in postural adaptation. This may be due to the reciprocal connections which exist between the bilateral PPC and the cerebellum [258]. Specifically the IPL, which compares perceived body positions to extra personal space is innervated by the cerebellum [259]. The PPC utilizes sensory feedback as well as the efferent copy provided by the cerebellum to maintain an internal representation of limb positions and the body in space, what could be described as body ownership or the body schema [258,260–263]. Recent publications have even gone so far as to identify the PPC as the home for the "posture cells of the brain" [33,34]. The current study reinforces the notion of the bilateral PPC's role in monitoring and updating the internal representation.

This investigation identified decreased postural adaptation following cathodal stimulation of either the left or right hemisphere of the PPC. This study employed a paradigm which stimulated the bilateral PPC in lieu of placing the return electrode on another brain region (i.e. the supraorbital foramen) [230] in order to contain stimulation to the PPC and not alter excitability of other brain regions such as the somatosensory or motor cortices. Because of this, as one hemisphere received inhibitory stimulation, the other received excitatory stimulation. Previously, some studies have shown that healthy young subjects experience alteration of sensory detection thresholds following cathodal, but not anodal stimulation of S1 [252]. Additionally, it has been shown that cathodal stimulation of the cerebellum decreases postural stability while anodal does not change stability in young subjects [253]. While the effects of anodal stimulation on the contralateral hemisphere cannot be unequivocally ruled out, there is evidence that in healthy, young adults, anodal stimulation may not alter behavioral outcomes compared to Sham. Therefore, this study asserts that decreased postural adaptation is most likely due to the inhibitory nature of cathodal stimulation. Disruptive TMS may be employed in the future in order to confirm these findings because the more focal stimulation is less likely to alter excitability of other brain regions.

Although this this study involved neuromodulation of the PPC, no recordings of brain activity were obtained. Future investigations are needed to verify the effects of tDCS on PPC excitability in postural adaptation. This study is important because while upper body motor adaptation research is critical for understanding the dynamics of human sensorimotor control, postural adaptation is more directly linked to public health due to fall risk. Therefore, this investigation provides novel information which may lead future experimentation to what efficacy there may be for non-invasive brain stimulation as a therapeutic measure to improve adaptability during postural control, decreasing fall risk. Future investigations should include clinical populations to identify the viability of tDCS of the PPC as a rehabilitative mechanism as well as include neuroimaging techniques.

Conclusions

Conclusions. The results of this dissertation achieved three primary findings:

1. **Alteration of support surface characteristics alters responses to vibration.**

Vibration of the tibialis anterior which occurred on an inclined surface did not exhibit the anterior shift associated with typical TA vibration (Fig 12). While the most likely cause of this phenomenon is mechanical, this investigation also identified that Achilles tendon vibration's effects are muted during lean after-effect (Fig 13). This shows evidence of the ability of the system to exhibit multiple adaptations of the same channel at the same time. Together, these results also demonstrate that AT and TA vibration should not be considered identical, if mirrored, phenomenon and that researchers must be aware of the contexts of vibration which may influence their effects.

2. **Shank vibration can alter LAE in some contexts.**

Vibration of either the TA or AT during inclined stance did not alter LAE (Fig 15). Based on previous suggestions that the magnitude of LAE is affected by proprioceptive weighting, and because vibration is commonly accepted to decrease proprioceptive reliability, it was expected that vibration during T2 would decrease LAE magnitude. This did not happen, providing opposition to the notion that proprioceptive reliability, and therefore weight, is strongly related to lean after-effect. Vibration during the lean after-effect period (T3), had immediate and profound impacts on COG position (Fig 16). This finding demonstrated that vibration is a stronger sensory alteration than an incline-intervention. Together, these results improve our understanding of lean after-effect and our general understanding of postural adaptation as it relates to dynamic sensory reweighting.

3. **Non-invasive brain stimulation of the posterior parietal cortex alters postural adaptation.**

Inhibitory (cathodal) stimulation of the either hemisphere of the PPC decreased postural adaptation (Fig 20 & 21). Both active stimulation conditions exhibited decreased LAE measured at two time periods. Maximum and Average LAE during the Late period were both decreased following active stimulation. Off-set time was not changed suggesting that inhibitory stimulation of the PPC decreased initial adaptation rather than recalibration following adaptation.

Synthesis.

The result of these findings together improves our understanding of postural adaptation as well as sensory integration both from a behavioral and cortical level. These results will inform future studies focusing on postural adaptation. The role of sensory perturbations on postural adaptations such as lean after-effect requires more extensive investigation in clinical populations. Furthermore, the role of the PPC in adaptation to repeated bouts of sensory perturbations (i.e. repeated exposures to vibration), as well as consolidation or potential retention or transfer of learned responses to vibration or other sensory perturbations during stance is yet unknown. The correlation of postural and visuomotor adaptability with or without stimulation of the PPC is also an unresolved question.

Implications. This dissertation investigated basic scientific questions regarding postural adaptation which was conducted in order to improve our general understanding of the neurological basis of human movement. Results of this investigation improve our basic understanding of how postural adaptation occurs and what may influence adaptability. Adaptability of the body schema is crucial for successfully navigating a world that is constantly changing. This dissertation highlighted the potential for training meant to improve sensory reweighting capabilities to improve adaptability. Furthermore, this dissertation highlighted the potential for the addition of non-invasive brain stimulation designed to improve function of the posterior parietal cortex to improve adaptability. If results of this investigation can be generalized to those with deficits in adaptability, it is possible that stimulation designed to improve functionality of the PPC can decrease fall risk.

Limitations. As with any investigation, this dissertation is not without limitations. First and foremost, while healthy young subjects are a convenient sample that are useful for performing basic sensorimotor control science like in set of investigations, generalization to any specific clinical population such as the elderly, or those with dementia stroke or Parkinson's, is not possible. Similarly, while tDCS is known to alter activity of areas under anodal and cathodal electrode(s), no neuroimaging was performed in this investigation to confirm alterations in excitability induced by tDCS or to correlate brain activity with performance in any measure.

Future Directions. Future research should seek to expand this line of research and address the limitations of the current set of experiments. Future investigations should attempt to identify whether sensory reweighting training can improve postural adaptability in order to decrease fall risk in clinical populations. Future investigations should also utilize neuromodulation of the PPC in order to identify effects on other forms of adaptation (i.e. during gait) or on motor learning applications. Other stimulation techniques may be advisable to pinpoint the specific roles of the hemispheres of the PPC or sub-regions of the PPC.

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APPENDIX

UNIVERSITY of HOUSTON

A CARNEGIE-DESIGNATED TIER ONE PUBLIC RESEARCH UNIVERSITY

CONSENT TO TAKE PART IN A HUMAN RESEARCH STUDY

Title of research study: Effects of Tendon Vibration on Lean After-Effect
Investigator: **David Young under the supervision of Dr. Charles Layne**

Key Information:

The following focused information is being presented to assist you in understanding the key elements of this study, as well as the basic reasons why you may or may not wish to consider taking part. This section is only a summary; more detailed information, including how to contact the research team for additional information or questions, follows within the remainder of this document under the "Detailed Information" heading.

What should I know about a research study?

- Someone will explain this research study to you.
- Taking part in the research is voluntary; whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide, and can ask questions at any time during the study.

We invite you to take part in a research study about the effects of tendon vibration on balance because you meet the following criteria: Healthy young adult between the ages of 18-35 with no neurological or physical disability which impairs your posture.

In general, your participation in the research involves undergoing six bouts of inclined-stance (i.e. standing with your toes on an incline) followed by a post-test. During these bouts you will experience vibration on the front or back of your lower legs.

The primary risk to you in taking part is irritation from the mechanical vibrators or the adhesive placed upon your skin for motion capture. There is no personal benefit, however the benefit to society may be an improved understanding of postural adaptation which may be used to improve rehabilitation techniques. You will receive compensation for participation. Instead of being in this research study, you may choose to not participate.

Detailed Information:

The following is more detailed information about this study, in addition to the information listed above.

Why is this research being done?

The purpose of this research is to better understand human balance control. It is believed that we use sensory feedback to achieve balance, which is how the brain decides which sense (e.g. vision or touch etc) to trust more to help guide its decisions. We are interested to see how tendon vibration influences this phenomenon. While you are unlikely to receive any benefit from participation in this study, the information which is discovered by this study may help with rehabilitation in postural control in disabled populations.

How long will the research last?

We expect that you will be in this research study for three visits. The first visit will require roughly one hour and the following two visits will require roughly ninety minutes. Visits must be spaced out a minimum of 48 hours.

How many people will be studied?

We expect to enroll about fifteen people in this research study.

What happens if I say yes, I want to be in this research?

If you say yes, you want to be in this research, you will undergo six data collection sessions which will occur over three separate days. For each task, your eyes will be closed and your arms crossed in front of your body. You will also wear noise canceling ear muffs. During the first session you will be asked to perform four tasks. First, you will be asked to perform a Baseline Trial- 30 seconds of quiet standing. Next, you will be asked to perform a Limits of Stability trial, three tries to lean as far forward as you can. Next, you will be asked to perform an Incline-Intervention Trial, 5 minutes of standing on a surface inclined at 10-degrees. Last, you will be asked to perform a Post-Test Trial, five minutes of standing on a flat surface. For visits two and three, you will be exposed to two conditions each. Each additional condition involves the Baseline Trial, Incline-Intervention Trial, and Post-Test Trial. For each condition of the second two visits, you will be exposed to tendon vibration on the front or back of your shin during either the Incline-Intervention Trial or the Post-Test Trial. In between the two collection sessions which occur on Day 2 and Day 3, you will be asked to undergo a thirty minute “Washout” period, during which you may relax, study, or do whatever you wish. Prior to each session you will be outfitted with reflective markers so that our infrared camera system can measure the movement of your body. These cameras only capture markers and do not capture your image. You are likely to interact with the PI (David Young) and may interact with research assistants. The research will be performed in the Motion Analysis Lab at the Center for Neuromotor and Biomechanics Research which is located in Health and Science Building 2 in Room 2051. The research will be completed at times agreed upon by the research staff and subject.

What happens if I do not want to be in this research?

You can choose not to take part in the research and it will not be held against you. Choosing not to take part will involve no penalty or loss of benefit to which you are otherwise entitled.

If you are a student, a decision to take part or not, or to withdraw from the research will have no effect on your grades or standing with the University of Houston.

What happens if I say yes, but I change my mind later?

You can leave the research at any time it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can remove any future appointments and remove data from any planned analyses. There is no need to explain the reason for withdrawal. If you stop being in the research, already collected data will be removed from the study record.

Is there any way being in this study could be bad for me?

Reflective markers will be placed on your clothing and on your skin. Markers placed on your skin will be secured with tape. When this tape is removed, there is the potential for irritation and mild pain, similar to that of removing a band aid.
There are no other foreseeable risks related to the procedures conducted as part of this study. If you choose to take part and undergo a negative event you feel is related to the study, please inform your study team. Taking part in this research study may lead to added costs to you. If you do not have a campus parking permit, you may pay for parking in the lot adjacent to our laboratory. This is not mandatory if the subject can provide their own transportation to the laboratory or has a parking permit.

Will I receive anything for being in this study?

To express our gratitude for your taking part in the research process, you will receive a $20 gift card to Target upon completion of all data collection sessions.

Will being in this study help me in any way?

There are no known benefits to you from your taking part in this research. However, possible benefits to others include improved understanding of postural adaptation and potential improvement of rehabilitation techniques.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. Each subject's name will be paired with a code number, which will appear on all written study materials. The list pairing the subject's name to the assigned code number will be kept separate from these materials. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization, as well as collaborating institutions and federal agencies that oversee human subjects research. We may publish the results of this research. However, unless otherwise detailed in this document, we will keep your name and other identifying information confidential.

We may share and/or publish the results of this research. However, unless otherwise detailed in this document, we will keep your name and other identifying information confidential.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, you should talk to the research team at dyoung6@uh.edu or (301) 418-5747

This research has been reviewed and approved by the University of Houston Institutional Review Board (IRB). You may also talk to them at (713) 743-9204 or cphs@central.uh.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Your signature documents your consent to take part in this research.

____________________ Signature of subject	__________ Date
____________________ Printed name of subject	
____________________ Signature of person obtaining consent	__________ Date
____________________ Printed name of person obtaining consent	

UNIVERSITY of HOUSTON
A CARNEGIE-DESIGNATED TIER ONE PUBLIC RESEARCH UNIVERSITY

CONSENT TO TAKE PART IN A HUMAN RESEARCH STUDY

Title of research study: Effects of tDCS of the PPC on Lean After-Effect
Investigator: **David Young under the supervision of Dr. Charles Layne**

Key Information:

The following focused information is being presented to assist you in understanding the key elements of this study, as well as the basic reasons why you may or may not wish to consider taking part. This section is only a summary; more detailed information, including how to contact the research team for additional information or questions, follows within the remainder of this document under the "Detailed Information" heading.

What should I know about a research study?

- Someone will explain this research study to you.
- Taking part in the research is voluntary; whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide, and can ask questions at any time during the study.

We invite you to take part in a research study about the effects of transcranial direct current stimulation (tDCS) of the posterior parietal cortex (PPC) on postural adaptation because you meet the following criteria: Healthy young adult between the ages of 18-35 with no neurological or physical disability which impairs your posture and right-foot dominance.

In general, your participation in the research involves undergoing three bouts of inclined-stance (i.e. standing with your toes on an incline) followed by a post-test. Prior these bouts you will experience tDCS stimulation.
The primary risk to you in taking part is irritation from the transcranial direct current stimulation (tDCS) stimulation or the adhesive placed upon your skin for motion capture. There is no personal benefit, however the benefit to society may be an improved understanding of postural adaptation which may be used to improve

rehabilitation techniques. You will receive compensation for participation. Instead of being in this research study, you may choose to not participate.

Detailed Information:

The following is more detailed information about this study, in addition to the information listed above.

Why is this research being done?

The purpose of this research is to better understand the process of postural adaptation. It is believed that postural adaptation may be influenced by sensory integration, which is how the brain is able to make sense of multiple pieces of information (e.g. vision or touch etc) to help guide its decisions. We are interested to see how tDCS stimulation influences adaptation. While you are unlikely to receive any benefit from participation in this study, the information which is discovered by this study may help with rehabilitation in postural control in disabled populations.

How long will the research last?

We expect that you will be in this research study for three visits. The first visit will require roughly 90 minutes and the following two visits will require roughly 60 minutes. Visits must be spaced out a minimum of 48 hours.

How many people will be studied?

We expect to enroll about twenty people in this research study.

What happens if I say yes, I want to be in this research?

If you say yes, you want to be in this research, you will undergo three data collection sessions which will occur over three separate days. For each task, your eyes will be closed and your arms crossed in front of your body. You will also wear noise canceling ear muffs. During the first session you will be asked to perform four tasks. First, you will be asked to perform a Baseline Trial- 30 seconds of quiet standing. Next, you will be asked to perform a Limits of Stability trial, three tries to lean as far forward as you can. Next, you will be asked to perform an Incline-Intervention Trial, 5 minutes of standing on a surface inclined at 10-degrees. Last, you will be asked to perform a Post-Test Trial, five minutes of standing on a flat surface. For visits two and three, you will undergo one additional condition each. Each additional condition involves the Baseline Trial, Incline-Intervention Trial, and Post-Test Trial. Prior to each condition (all three visits) you will be exposed to tDCS stimulation. In a randomized order, you will experience sham (placebo), cathodal (negative) and anodal (positive) stimulation. Also prior to each session you will be outfitted with reflective markers so that our infrared camera system can measure the movement of your body. These cameras only capture markers and do not capture your image. You are likely to interact with the PI (David Young) and may interact with research assistants. The research will be performed in the Motion Analysis Lab at the Center for Neuromotor and Biomechanics Research which is located in Health and Science Building 2 in

Room 2051. The research will be completed at times agreed upon by the research staff and subject.

What happens if I do not want to be in this research?

You can choose not to take part in the research and it will not be held against you. Choosing not to take part will involve no penalty or loss of benefit to which you are otherwise entitled.

If you are a student, a decision to take part or not, or to withdraw from the research will have no effect on your grades or standing with the University of Houston.

What happens if I say yes, but I change my mind later?

You can leave the research at any time it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can remove any future appointments and remove data from any planned analyses. There is no need to explain the reason for withdrawal. If you stop being in the research, already collected data will be removed from the study record.

Is there any way being in this study could be bad for me?

Reflective markers will be placed on your clothing and on your skin. Markers placed on your skin will be secured with tape. When this tape is removed, there is the potential for irritation and mild pain, similar to that of removing a band aid.

There is a risk of irritation from the transcranial direct current stimulation (tDCS) stimulation. Specifically, a slight tingling sensation is often reported during the early moments of stimulation. This stimulation typically dissipates in less than a minute. tDCS stimulation has been shown to be safe and well tolerated in healthy individuals (for review, see Antal et al., 2017). Previously Matsumoto and Ugawa found that no serious adverse effects have been reported in experiments using tDCS. tDCS stimulation involves the placement of saline soaked sponges on the scalp. Because of this, you should be prepared to have your hair slightly wetted.

There are no other foreseeable risks related to the procedures conducted as part of this study. If you choose to take part and undergo a negative event you feel is related to the study, please inform your study team. Taking part in this research study may lead to added costs to you. If you do not have a campus parking permit, you may pay for parking in the lot adjacent to our laboratory. This is not mandatory if the subject can provide their own transportation to the laboratory or has a parking permit.

Will I receive anything for being in this study?

To express our gratitude for your taking part in the research process, you will receive a $20 gift card to Target upon completion of all data collection sessions.

Will being in this study help me in any way?

There are no known benefits to you from your taking part in this research. However, possible benefits to others include improved understanding of postural adaptation and potential improvement of rehabilitation techniques.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. Each subject's name will be paired with a code number, which will appear on all written study materials. The list pairing the subject's name to the assigned code number will be kept separate from these materials. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization, as well as collaborating institutions and federal agencies that oversee human subjects research. We may publish the results of this research. However, unless otherwise detailed in this document, we will keep your name and other identifying information confidential.

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This research has been reviewed and approved by the University of Houston Institutional Review Board (IRB). You may also talk to them at (713) 743-9204 or cphs@central.uh.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

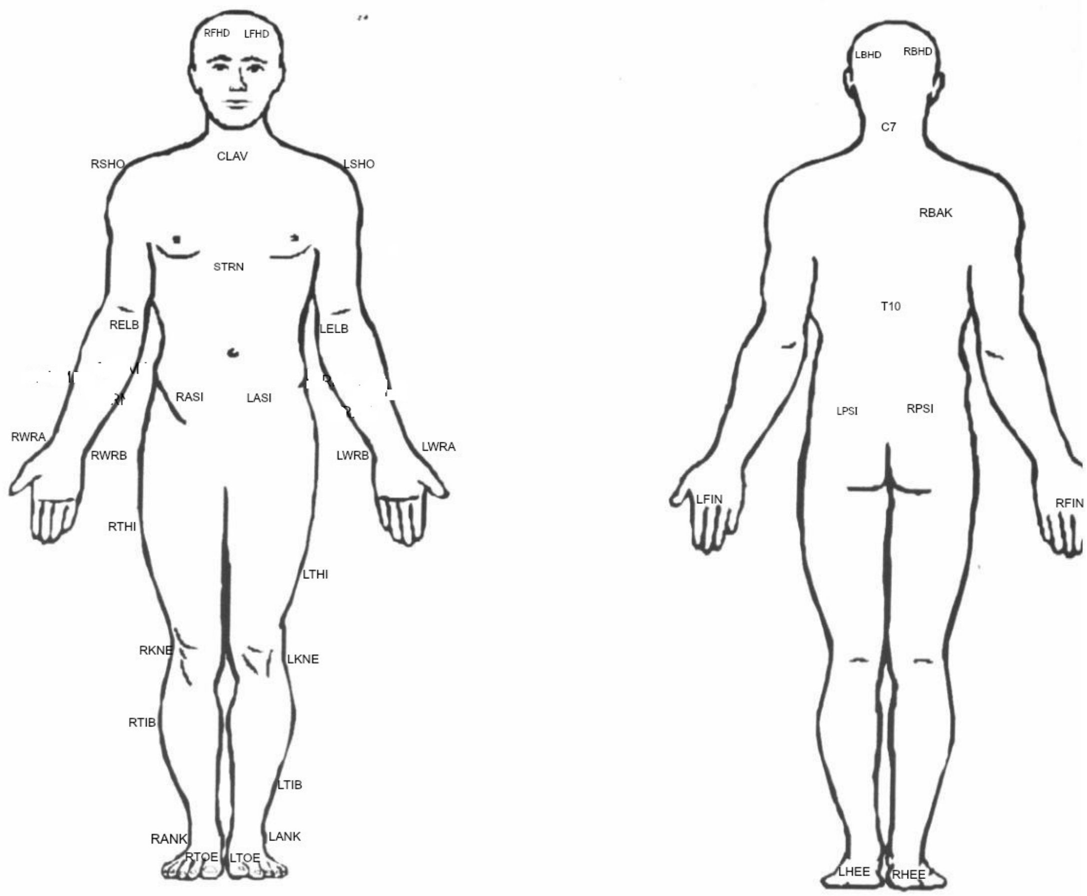
Your signature documents your consent to take part in this research.

Signature of subject ____________________ Date ____________

Printed name of subject ____________________

Signature of person obtaining consent ____________________ Date ____________

Printed name of person obtaining consent ____________________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RKNE
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RTOE
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LBHD
RBHD
C7
RBAK
T10
LPSI
RPSI
LFIN
RFIN
LHEE
RHEE

Modified Physical Activity Readiness Questionnaire (PAR-Q)

Participant Name:	Date:

For most people physical activity should not pose any problem or hazard. PAR-Q has been designed to identify the small number of adults for whom physical activity might be inappropriate or those who should have medical advice concerning the type of activity most suitable for them. Common sense is your best guide in answering these few questions. Please read them carefully and mark the yes or no opposite the question as it applies to you.

Yes	No	1) Has a physician ever said you have a heart condition and you should only d physical activity recommended by a physician?
Yes	No	2) When you do physical activity, do you feel pain in your chest?
Yes	No	3) In the past month have you had chest pain when you were not doing physica activity?
Yes	No	4) Do you lose your balance because of dizziness or do you ever lose consciousness?
Yes	No	5) Do you have a joint or a bone condition or problems with your feet? If so, specify:
Yes	No	6) Do you have insulin dependent diabetes or related conditions? If so, specify:
Yes	No	7) Do you have any breathing difficulties or suffer from asthma?
Yes	No	8) Do you suffer from epilepsy?
Yes	No	9) Do you have any neurological conditions? If so, specify:
Yes	No	10) Have you had a major operation? If so, specify (what, when):
Yes	No	11) Do you suffer from any other medical conditions? If so, specify:
Yes	No	12) Do you know of any other reason you should not exercise or increase your physical activity?
Yes	No	13) Are you using any medication currently or have been using any in the last week? If so, what kind of medication did you use?
Yes	No	14) Are you unable to stand upright for four to five minutes?

<table>
<tr><th colspan="4">Experiment 1 & 2</th></tr>
<tr><td colspan="2">Subject:
Date:</td><td colspan="2">Informed Consent:
PAR-Q:</td></tr>
<tr><td>Equipment Preparation:
Vicon hardware
Vicon software
35 marker set</td><td>Extra tape
Ankle stretcher
VB115s
Stop watch
Headphones</td><td>Age:
Height:
Weight:
Leg length:
Knee width:</td><td>Ankle width:
Shoulder offset:
Elbow:
Wrist:
Hand:</td></tr>
<tr><td colspan="2">First protocol:
Set auto capture to 300s
Limits of stability
Baseline trial 30 seconds
Incline trial 5* for 300s
Post-test trial 300s</td><td colspan="2">Randomized condition order:
C1= Baseline
C2=Gastroc during incline
C3= Tib during incline
C4= Gastroc during post-test
C4= Tib during post-test
Order:
Completed:</td></tr>
</table>

<table>
<tr><th colspan="4">Experiment 3 Data Sheet</th></tr>
<tr><td colspan="2">ID Number:
Date (first):
Date (second):
Date (third):</td><td colspan="2">Informed Consent:
PAR-Q:
Age: Sex:</td></tr>
<tr><td>Equipment Preparation:
Vicon hardware
Vicon software</td><td>Extra tape
Ankle stretcher
Neurolectrics tDCS
Headphones</td><td>Height:
Weight:
Leg length:
Knee width:
Ankle width:</td><td>Shoulder offset:
Elbow:
Wrist:
Hand:</td></tr>
<tr><td colspan="2">First protocol:
Explanations
Calibration (tape feet)
Baseline trial (auto to 30)
Incline trial 5* (auto to 300)
Post-test trial (close eyes after 5s)
Vibration Trials (auto to 65)
SB Trials (auto to 180)</td><td colspan="2">Randomized condition order:
C1= Sham stimulation
C2= Anodal stimulation
C3= Cathodal stimulation
Order:
V1 Guess:
V2 Guess:
V3 Guess:</td></tr>
</table>