INFLUENCE OF VESTIBULAR SENSORY ILLUSION ON ACUTE AND ADAPTIVE POSTURAL RESPONSES IN INDIVIDUALS WITH PARKINSON DISEASE AND HEALTHY CONTROLS

by

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ABSTRACT

Integration of sensory inputs by the central nervous system (CNS) is necessary for adequate postural stability, but diminishes with age and is further impaired in Parkinson disease (PD). As a result, the CNS cannot appropriately weight sensory stimuli to facilitate postural responses to sudden changes in sensory input. Training the sensorimotor system to ignore or rapidly adapt to aberrant postural cues may improve postural control in PD.

We evaluated the influence of acute and repeated exposure to galvanic vestibular stimulation (GVS) on postural responses during static and dynamic tasks to determine whether training improved these responses. We hypothesized that individuals with PD would demonstrate impaired postural recovery responses to acute GVS relative to healthy controls and that individuals with PD and healthy elders would demonstrate diminished adaptive responses to repeated GVS compared to young adults.

Twelve individuals with PD (PD group), 15 healthy young adults (HY group), and 11 healthy elders (HE group) participated. Timing of GVS was randomly applied during each task. Fifteen acquisition and nine retention trials with GVS were compared to assess learning.

The PD group took longer to stabilize their center of pressure (COP) in quiet stance following GVS acutely compared to controls. The PD and HE groups had lower sample entropy (SaEn) compared to the HY. Neither the PD nor HE groups

demonstrated changes in SaEn or meaningful improvements in postural control during acquisition or retention. SaEn in the HY group acutely decreased and then increased at retention which coincided with a meaningful improvement in postural control.

The PD group had impaired motor planning, postural preparation, and postural stability during a rise to toes task following acute GVS, but these constructs returned to baseline at later acquisition and retention time points. Controls suppressed GVS acutely.

Postural coordination decreased acutely in the PD group during tether release. This persisted and an adaptive trend in BOS transition was noted with repeated GVS exposure in this group. No changes were observed in the control groups.

Taken together, these results demonstrated that acute GVS differentially affects postural control in individuals with PD. Our results support the hypothesis that reweighting of sensory stimuli is impaired in PD. We also show that individuals with PD are able to suppress attention to a vestibular illusion and demonstrate adaptive responses to a postural threat.

This dissertation work is dedicated to my mother, Joyce Evelyn Lester, who taught me the joy of exploring and the importance of learning, and to my beautiful wife Holly, who lit a candle in my heart and gave me the inspiration to never settle for less than the fulfillment of my dreams.

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CHAPTER 1

INTRODUCTION

Parkinson disease (PD) is a progressive neurodegenerative disorder whose motor deficits result from loss of dopaminergic neurons in the basal ganglia, particularly within the substantia nigra pars compacta.[1] It is the second most common neurodegenerative disease, with a worldwide prevalence of 0.1-0.3% per 100,000 and rising prevalence associated with aging.[1,2] The clinical presentation of PD includes hallmark motor signs of tremor, rigidity, akinesia, bradykinesia, and postural instability. Among the motor signs, postural instability has the most serious implications for morbidity and mortality due its relationship with injurious falls leading to fracture, reduced mobility, and functional decline.[3-5] Fall risk among individuals with PD is twice that of age-matched controls, occurring in 51% to 68% of those with the disorder.[6] Individuals with PD who fall are at 1.62 (CI_{95} = 1.24-2.13) times the risk for hip fracture.[7] Sixty-nine percent of individuals with PD who sustain a hip fracture require placement in a skilled nursing facility, and as many as 94% are unable to walk more than 200 m 2 years after surgical repair of their injury.[8] Strategies to improve postural control in this population and prevent falls are critically needed.

Postural stability is predicated upon the central nervous system's ability to produce appropriate motor responses to a changing external environment. Individuals with Parkinson disease (PD) demonstrate impairments in postural control that have

limited ability to improve with pharmacologic therapy[9] or surgical intervention[10] and tend to worsen with disease progression. While the etiology of postural instability in PD is multifactorial, it is related to rigidity, bradykinesia, muscle weakness, and impairment of sensory integration.[5,11-13]

Sensory integration is the timely and accurate compiling of sensory information from the visual, somatosensory, and vestibular systems to produce a context appropriate motor response and optimize postural control in a changing physical environment.[14] The postural control system relies on the redundancy of information from these sensory systems in order to correctly distinguish self-motion from motion in the environment and generate appropriate postural resposnes.[15] In PD, impairment of sensory integration has been most clearly demonstrated by proprioceptive-specific deficits,[12,16,17] which are believed to be directly associated with the degradation of dopaminergic pathways.[12] However, sensory integration deficits in PD are compounded by normal age-associated deficits, which, in turn, are influenced by age-related declines in each modality.[18]

Impaired sensory integration necessarily leads to a diminished adaptive ability to respond to sudden changes in sensory input. This ability is known as sensory reweighting and is both the means by which acute control of postural stability is administered and a necessary skill to prevent falls.[19-21] Sensory reweighting is of particular importance when modality-specific information is in conflict with information from other modalities. When this occurs, the central nervous system functions to downregulate inaccurate sensory cues and upregulate accurate cues in order to maintain postural equilibrium.[22] For instance, imagine looking at the horizon while standing on the bow of a boat being rocked by waves. In this scenario, visual information (the constant line of the horizon) is

in conflict with somatosensory information (the changing position of the lower extremity joint angles as the boat rocks) and vestibular information (the acceleration of the head on the body and the body in space to the movement of the boat). If all sensory modalities were weighted the same or if vision were downregulated, the result would be that you would stumble or fall as you attempted to correct your head on body or body in space orientation, or you would become nauseous and everyone on the boat would subsequently enjoy watching all the colorful fish in the area nibble on whatever you had for lunch earlier in the day. What happens instead is that vision is upregulated and the other sensory cues downregulated by your postural control system in order to maintain a vertical head / eye alignment with the horizon while your body is allowed to sway with the boat - a phenomenon known as a visual sway reference.

Since age-related changes diminish sensory modalities and thus the redundancy between them, the ability to reweight sensory stimuli declines with age as well;[18-21] similarly, modality-specific impairments in PD contribute to impaired reweighting in these individuals as well.[23,24] These deficits may result in an overreliance on remaining sensory modalities in an attempt to produce appropriate motor responses to perturbation.[25,26] As a result, these individuals are more susceptible to falls following perturbation of one or more of the sensory modalities that regulate postural stability because less information is available to be evaluated for comparative accuracy.[23,24,27] Theoretically, it would be desirable to integrate existing balance training initiatives, which tend to focus on the motor component of postural control, with training individuals to reweight aberrant sensory cues in order to facilitate a more functional sensorimotor adaptation to postural disturbances. However, the ability to train the sensorimotor system

to ignore or rapidly adapt to aberrant postural cues is understudied and needs to be better understood before such a theoretical goal can be realized.

Sensory reweighting can be most readily studied experimentally through provocation of a sensory conflict, that is manipulating one or more sensory systems to reduce the amount or accuracy of the information it provides (ie, altering visual and proprioceptive input by having a person close their eyes and stand on a foam surface).[28] This manipulation is called a sensory illusion. When one sensory modality is impaired, manipulating the remaining intact modalities provides information on the extent of the deficit or the adaptability of the overall system.[29] Postural responses in PD to somatosensory and visual sensory conflict are well defined.[30-34] However, the influence of vestibular conflict on postural control in this population is less apparent.

Sensory illusions of the vestibular system are commonly evoked in research settings using galvanic vestibular stimulation (GVS), which provides a means of selectively producing vestibular illusions by using a low amplitude electrical impulse to stimulate the afferent limb of the vestibular nerve and evoke the sensation of a change in head on body orientation.[35,36] This in turn produces a compensatory response of the head and body to counteract the perceived movement. As an example of nervous system adaptation to sensory changes, sensitivity to GVS is increased in individuals with diminished peripheral somatosensation.[37] Additionally, short term adaptive changes[38] and motor learning effects,[39] as evidenced by decreasing center of pressure (COP) variability, have been demonstrated following repeated exposure to GVS. In a single study, individuals with PD were shown to have a similar (though exaggerated) acute response to GVS application during quiet stance compared to controls.[40] It is currently

unknown, however, how recovery of postural control following cessation of this type of sensory illusion is influenced acutely in PD where sensory integration is impaired or whether adaptive changes may occur with repeated exposure, given the deficits in motor learning associated with the disease.[41]

In order to study adaptation to sensory conflict thoroughly, it is expedient to investigate traditional linear measures (eg, COP position and variability) and, where possible, nonlinear components of postural control. Postural control is comprised of both stochastic and dynamic processes, which interact to produce purposeful movement and maintain a dynamic equilibrium of the body in space.[42] Nonlinear tools consider the variability associated with movement to contain meaningful information about how the postural control system interacts with the environment, which allows the system to develop flexible and adaptive strategies to maintain stability.[43]

The principle goal of this dissertation project was to determine the influence of acute and repeated exposure to vestibular sensory illusions on sensory reweighting and to lay the groundwork toward developing evidence-based sensorimotor adaptation paradigms to improve postural control in PD. The general purpose of these studies was to determine whether repeated exposure to aberrant vestibular sensory cues differentially affected acute and/or adaptive postural recovery responses among individuals with PD and neurologically healthy young and older adults. Our overall hypothesis was that despite progressive impairments in sensory reweighting between healthy elders and persons with PD compared to healthy young adults, repeated exposure to sensory illusions will result in the learning of a more appropriate pattern of COM and COP control across and within all groups. To meet this end, we developed the following

specific aims:

Specific Aim 1: Examine the acute effects of vestibular sensory illusions on postural coordination and the time course of postural stabilization.

Specific Aim 2: Examine the acquisition and retention of postural stabilization in response to repeated exposure to a vestibular sensory illusion during stereotyped balance tasks.

In order to accomplish our overall purpose and test our general hypothesis and specific aims, we conducted a series of experiments evaluating static (quiet standing), anticipatory (rise to toes), and reactive (tether release) postural tasks. These studies and their rationale are briefly described below, and their detailed description is provided in the chapters that follow.

Vestibular Sensory Conflict Reweighting During Quiet Stance

Previous research has characterized center of pressure changes associated with sensory illusions.[35,38,44-47] Additionally, day to day adaptation to GVS has been demonstrated in young healthy individuals following five training sessions.[39] To date, the deterministic nature and complexity of movement variability associated with induced vestibular sensory illusions has not been characterized. Additionally, adaptive responses to repeated exposure to GVS in individuals with PD or healthy older adults have not been reported.

Our first investigation, therefore, aimed to evaluate the influence of repeated exposure to vestibular sensory illusions during quiet stance on postural recovery, comparing individuals with PD to healthy young and age-matched controls. Specifically, we sought to address the following aims: 1) Do age or Parkinson disease differentially

affect postural recovery to vestibular sensory conflict acutely (eg, within trials); 2) Do age or Parkinson disease differentially affect adaptation of postural control following repeated exposure to a vestibular sensory conflict (eg, between trials within and between days); and 3) Does postural recovery from a vestibular sensory illusion occur in a predictable and similar time course, regardless of age or Parkinson disease? We hypothesized that individuals with Parkinson disease would demonstrate an impaired postural recovery response to acute GVS exposure and that both individuals with PD and older healthy adults would demonstrate less robust adaptive responses to repeated GVS exposure. We further hypothesized that postural recovery following GVS would occur in a predictable time course regardless of age or PD.

Vestibular Sensory Conflict Reweighting During Rise to Toes

The context in which the sensory conflict is evoked may affect both the acute and adaptive responses to the sensory illusion. Previous research has shown that the timing of GVS during step initiation differentially affects subsequent postural responses in healthy adults.[48] Postural responses to a vestibular sensory illusion during a more challenging anticipatory postural task, however, have not previously been reported. Clearly, in order to better understand how sensory reweighting is affected in PD, it is important to evaluate the spectrum of sensory systems involved in postural stability and determine the magnitude of reweighting deficits across a variety of static and dynamic postural tasks.

Our second study, therefore, aimed to evaluate the influence of repeated exposure to vestibular sensory illusions during an anticipatory postural task on postural control, comparing individuals with PD to healthy young and age-matched controls. We

hypothesized that postural responses in individuals with PD would be smaller and slower during the anticipatory postural task (a rise to toes task [RTT]), compared to age-matched and healthy young controls. We further hypothesized that acute exposure to GVS would deleteriously affect postural responses in each group, but that subjects would adapt to the sensory illusion with repeated exposure and that individuals with PD would demonstrate less robust adaptive responses.

Vestibular Sensory Conflict Reweighting During Tether Release

In order to study the adaptability of PD to vestibular sensory illusions evoked by GVS, it is important to assess responses not only during static stance, but also during anticipatory and reactive tasks. While postural instability in PD is multidirectional,[49,50] it appears to be most pronounced posteriorly.[51,52] Unfortunately, few tests exist that assess posterior postural instability. Two such tests are the Pull Test (PT) and Posterior Push and Release Test (PPR), both of which are clinically based assessments. While these tests are hallmarks of clinical assessment in PD, they fail to allow adequate assessment of the underlying biomechanics that govern one's ability to recover balance by stepping. This lack of biomechanical detail severely limits any insights into the core characteristics of postural instability, rigidity, akinesia, bradykinesia, and hypokinesia and the effects of interventions targeted at these symptoms. A third test is the Posterior Tether Release (PTR), which is a laboratory based test and has been used to assess a number of underlying biomechanical characteristics associated with postural instability.[53]

As there have been no previous studies that have evaluated the coupling of tether release and altered sensory states, we undertook an additional study to determine whether repeated exposure to vestibular sensory illusions during a reactive postural control task

would influence postural responses differentially in PD subjects compared to healthy young and age-matched controls. We employed the PTR task to evoke reactive postural responses. The tether release has been used to evaluate postural responses to a simulated slip or trip in young and older populations.[54,55] We hypothesized that GVS would initially increase postural instability associated with tether release, but subjects would adapt to the sensory illusion over time. We further hypothesized that individuals with PD would demonstrate hypokinesia and bradykinesia compared to age-matched and healthy young controls.

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CHAPTER 2

ADAPTATION OF POSTURAL RECOVERY RESPONSES TO A VESTIBULAR SENSORY ILLUSION IN INDIVIDUALS WITH PARKINSON DISEASE AND HEALTHY CONTROLS

Abstract

The ability to reweight sensory stimuli to optimize postural stability diminishes with age and is further impaired by Parkinson disease (PD). Little is known, however, about the adaptive nature of sensory reweighting with training in these populations. The purpose of this study was to determine whether PD or age would differentially affect acute postural recovery or adaptive postural responses to novel or repeated exposure to a vestibular sensory illusion using GVS during quiet stance. In addition, we sought to determine the time course of postural recovery following a vestibular sensory illusion across groups. Postural instability increased within trials across all groups following application of GVS, but individuals with PD had a diminished capacity to stabilize their COP acutely following sensory illusion compared to controls. Both individuals with PD and age-matched controls demonstrated lower Sample Entropy (SaEn) than did young adults. Individuals with PD and healthy older adults failed to show increases in SaEn or clinically meaningful improvements in postural control with repeated exposure to GVS during acquisition and retention testing. In contrast, healthy young adults acutely changed their postural control behavior to the novel sensory illusion (by acutely changing from

high to low SaEn). This response persisted through acquisition; however, following a period of consolidation, SaEn increased in this group, which coincided with a clinically meaningful improvement in postural stability. Recovery of postural stability followed a similar time course across groups. Taken together, these results suggest that young adults learned to adapt to the sensory illusion in a more robust manner than older adults or those with PD. Further investigation into the nature of this adaptive difference is warranted.

Introduction

Individuals with Parkinson disease (PD) demonstrate impairments in postural control that may not improve with medical therapy.[1] Adequate postural control requires that the central nervous system integrate and adapt to sensory stimuli (eg, visual, proprioceptive, and vestibular) so that an appropriate motor response can be generated to maintain the center of mass (COM) within the base of support (BOS). Unfortunately, PD impairs the ability to integrate sensory inputs necessary for adequate postural stability in the face of external perturbation.[2-4] Inadequate sensory integration diminishes the central nervous system's ability to appropriately weight sensory stimuli to facilitate acute adaptive postural responses to sudden changes in sensory input.[5,6] Without appropriate sensory reweighting, individuals with PD are at greater risk of falls and fall associated morbidity.

Sensory reweighting can be most readily studied experimentally through the acute addition or subtraction of sensory input. Previous research has shown that individuals with PD experience deficits in reweighting when faced with proprioceptive[7] or visual illusions[2] and have a hyperkinetic response to acute vestibular illusion.[8] However, little is known about how persons with PD adapt their postural control in response to repeated

exposure to this type of sensory illusion. Galvanic vestibular stimulation (GVS) provides the ability to produce an isolated vestibular sensory illusion by stimulating the afferent limb of the vestibular nerve to evoke an illusory change in head on body orientation.[9] This in turn produces a compensatory response of the head and body to counteract the perceived movement. Vestibular stimulation, then, provides a unique tool with which to study an additional aspect of sensory reweighting.[9] Recent research in healthy young adults has demonstrated that repeated exposure to long duration GVS produces an adaptive response in the variability of center of pressure (COP), resulting in decreased sway variability to the sustained sensory illusion.[10] Little research has examined the acute response or the time course of recovery of postural stability following GVS in aged individuals or those with PD.

When adaptation to GVS-induced sensory illusions has been examined in these populations, the outcomes have generally been traditional linear measures of postural control such as COP position and variability changes. Since postural control is comprised of both stochastic and dynamic processes, which interact to produce purposeful movement and maintain a dynamic equilibrium of the body in space,[11] inclusion of linear and nonlinear outcomes is warranted. Nonlinear tools provide additional detail since they consider the variability associated with movement to contain meaningful information about how the postural control system interacts with the environment to develop flexible and adaptive strategies to maintain stability.[12]

This study, therefore, aimed to evaluate the influence of repeated exposure to vestibular sensory illusions during quiet stance on postural recovery, comparing individuals with PD to healthy young and age-matched controls. Specifically, we sought

to address the following aims: 1) Do age or Parkinson disease differentially affect postural recovery to vestibular sensory illusion acutely; 2) Do age or Parkinson disease differentially affect adaptation of postural control following repeated exposure to a vestibular sensory illusion; and 3) Does within trial postural recovery from a vestibular sensory illusion occur in a predictable and similar time course, regardless of age or Parkinson disease? We hypothesized that individuals with Parkinson disease would demonstrate an impaired postural recovery response to acute GVS exposure relative to neurologically healthy controls and that both individuals with PD and older healthy adults would demonstrate less robust adaptive responses to repeated GVS exposure than healthy young adults. We further hypothesized that postural recovery following GVS would occur in a predictable time course regardless of age or PD.

Methods

Participants

Three groups of participants were recruited for this study. These included 1) individuals with idiopathic Parkinson disease (PD group) recruited from a database of current and former patients in our movement disorders clinic; 2) healthy young adults (HY group) between the ages of 18 and 40 recruited from the university campus and surrounding community; and 3) healthy, elderly control participants (HE group) that were age-matched (±4 yrs) to the PD group and were recruited from the local community. Individuals with Parkinson disease (PD) who had not previously had surgical management of their symptoms and who had mild to moderate disease severity (Hoehn and Yahr scale score I-III) were included in the study. Additionally, all subjects had to be free of additional neurological impairment (ie, neuropathy, stroke, neuro-otologic

conditions, or traumatic brain injury) or recent major lower extremity orthopedic injury or disease (ie, fracture or severe osteoarthritis). Potential subjects who had lower extremity orthopedic surgical procedures within the previous 12 months were also excluded. Finally, all subjects had to be able to understand and follow instructions and not have any physical or cognitive limitation that prevented them from performing quiet stance or receiving GVS. Exclusion criteria were assessed by having potential subjects complete a self-report questionnaire of medical and surgical history (including questions on any history of inner ear injury or disease that affected balance) and undergo a screening examination that included reflex testing (recorded as absent, diminished, normal, or exaggerated), Semmes-Weinstein monofilament testing (recorded as present or absent using a 5.56 / 10g monofilament) to assess light touch perception, and quantitative vibration threshold testing using a Rydel Seiffer graduated tuning fork (recorded as normal or abnormal using a cutoff threshold of > 4 to be considered normal).

Instrumentation and Task

All testing was performed over 2 days in the Motion Capture Laboratory in our department using a 10-camera Vicon Motion Analysis System (Vicon Motion Systems, Centennial, CO, USA) and two AMTI OR6-7 series force platform (Advanced Medical Technologies Inc, Watertown, MA, USA). Participants were fitted with a standardized full-body gait analysis set of 55 reflective markers defining 15 body segments (Plug-In Gait marker set; Vicon Motion Systems, Centennial, CO) to quantify center of mass (COM) displacement and other kinematics during the task.

A quiet stance task was employed to compare acute and adaptive postural recovery responses to a vestibular sensory illusion across groups. Participants stood

quietly on a force plate in order to quantify center of pressure (COP) during the task. They stood with their head facing forward, their eyes open, and arms at their sides; heels were no more than 10 cm apart and toes angled outward approximately 20 degrees.

Bipolar galvanic vestibular stimulation (GVS) was applied over the bilateral mastoid processes using an isolated constant current stimulator (Grass Technologies, West Warwick, RI). A 1.5 mA, 50Hz stimulus was applied to each participant for 500 ms through 3 cm^2 electrode pairs with the cathode on the left side (Figure 2.1).

Procedures

All participants read and signed an informed consent document approved by the university IRB prior to participating in the study. Individuals with PD completed the motor component of the Movement Disorders Society Unified Parkinson Disease Rating Scale (MDS-UPDRS). Additionally, individuals in the PD and HE groups completed the functional gait assessment (FGA) in order to characterize their clinical balance and mobility. Subjects in the HY group were not required to complete the FGA because of potential ceiling effects associated with the instrument for individuals in this age group.

During testing, subjects wore form-fitting clothing and no shoes. Participant's height and weight were recorded. Butcher block paper was affixed to the force platform and tracings of the participant's feet were made on the paper to ensure all trials occurred from the same starting position. In order to evaluate postural responses associated with PD disease state and control for dopamine replacement medication effects, participants with PD were tested in an off-medication condition at least 12 hours after their last scheduled dosage.

A motor learning paradigm was employed in this study, using an acquisition

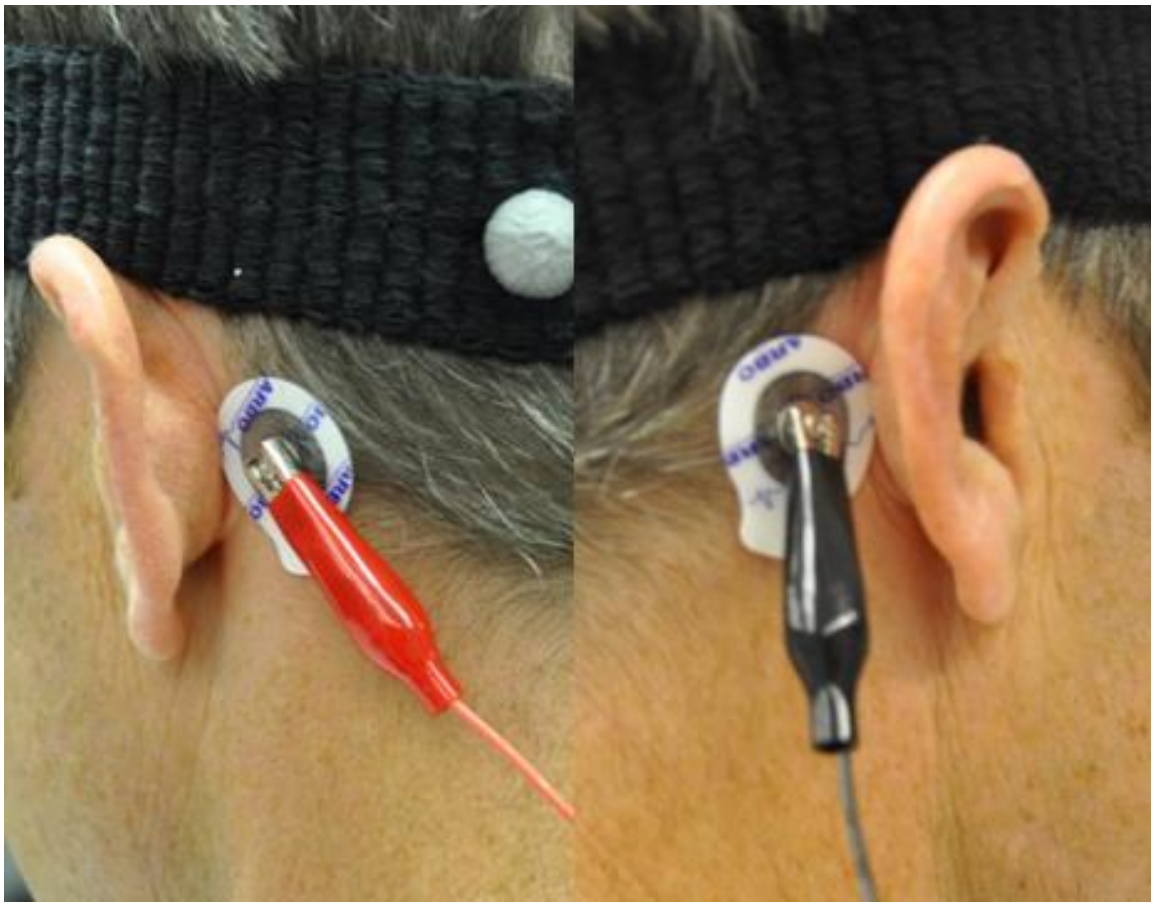

Figure 2.1 GVS Electrode Placement

phase and a retention phase.[13] During the acquisition phase (Day 1), participants completed 15 quiet stance trials with GVS, separated into five blocks of three trials. To avoid fatigue, participants were provided 30-second rest periods between each block of trials. During the retention phase (48 hours later), participants completed nine quiet stance trials with GVS, segregated into three blocks and including rest periods as previously described.

Each trial lasted approximately 25 seconds during which a vestibular sensory illusion was evoked approximately 6 seconds into the trial. A custom written Labview program (National Instruments Corporation Austin, TX, USA) randomly triggered vestibular stimulation within a 2-second window after at least 6 seconds of quiet stance data were collected. This paradigm was chosen to determine whether a vestibular-evoked sensory illusion would differentially influence acute postural recovery or postural adaptation over time in individuals with PD compared to healthy young and older controls. In order to prevent a fall if the participant was unable to maintain balance during the trial, a secondary restraint was worn and a spotter was present to assist balance recovery as needed.

Data Processing and Analysis

Kinematic (COM) and kinetic (COP) data were sampled at 200 Hz. Data were postprocessed using Vicon Nexus (Vicon Motion Systems, Centennial, CO, USA) and Visual 3D (C-Motion Inc, Germantown, MD, USA) software. To assess our primary linear outcomes of interest (COP CV; see below) kinetic and kinematic data were lowpass filtered at 15 Hz and 6 Hz, respectively, using a 4^{th} order zero phase lag Butterworth filter. The decision to use these filtering parameters was based on visual

inspection of the data and the residual analysis procedure for filter frequencies described by Winter.[14] Nonlinear outcomes of interest (SaEn; see below) were calculated from the raw data signal in order to prevent potential loss of temporal structure information and more accurately describe the system variability.[15]

Participant groups (PD group, HY group, and HE group) were compared across pre / poststimulation intervals and across performance phases (acquisition and retention). Within each trial, four time points surrounding the application of GVS comprised pre / poststimulation intervals. These included 3 seconds of quiet stance (QS) prior to stimulation, and three sequential 3-second intervals beginning at the cessation of GVS (eg, cessation to 3 seconds [GVS1], 3-6 seconds [GVS2], and 6-9 seconds [GVS3]). Four performance phase time points were used to compare differences in kinematic and kinetic variables across groups and pre- to poststimulation. These were 1) Acquisition Block-1 (EARLY), 2) Acquisition Block-3 (MID), 3) Acquisition Block-5 (LATE), and 4) Retention Block-2 (RET). The middle block of trials was chosen during retention to avoid transient motor learning factors such as warm-up decrement and fatigue from artificially influencing subject performance.[16]

Frontal plane head center of mass (ML-hCOM) position was utilized as a control variable. ML-hCOM was evaluated to ensure that GVS produced a repeatable postural disturbance across groups and time by comparing pre- to poststimulation intervals.

Average frontal plane body center of pressure coefficient of variation (ML-COP CV) was used to evaluate our principle aims, specifically whether acute within trial postural responses to GVS and adaptive postural control across trials following repeated exposure to sensory illusion differed across groups. The coefficient of variation was

calculated by dividing the center of pressure standard deviation by its mean at each pre / poststimulation time point across acquisition and retention for all groups. The coefficient of variation is a standardized measure of variability and was used to assess recovery of postural stability.[17] A larger CV was interpreted as reduced stability.

Sample Entropy (SaEn) of frontal plane COP (ML-COP) was the primary nonlinear outcome of interest. Sample entropy (SaEn) is a regularity statistic that provides insight into the complexity of the system being studied. It measures the regularity of repeating temporal segments of system output and provides an index of the degree of repeatability between two sequentially measured time segments.[18] The index ranges from 0 (completely regular / low entropy) to 2 (maximally irregular / high entropy). In a postural control context, SaEn provides understanding about how capable the system is of making flexible adaptations to environmental stresses based on how predictable a movement pattern is.[19] A pattern that is completely predictable (low SaEn) exhibits little if any complexity and suggests that the underlying postural control system has little adaptive flexibility. In contrast, a pattern that is highly unpredictable (high SaEN) and borders on randomness also exhibits little if any complexity and again suggests that the underlying system has little adaptive flexibility. In a healthy state, postural control output falls somewhere between these extremes, exhibiting an optimal amount of complexity to suggest that the underlying system can readily adapt to perturbations encountered in the environment. Calculation of SaEn requires three input parameters: 1) N, which is the number of data points being compared; 2) m, which is the length of the data window being compared; and 3) r, which is the similarity criterion.[20] A custom written program in Matlab (Mathworks, Natick, MA) was used to calculate

separate SaEn values for ML-COP from a 6-second period before (N = 1200) and another similar time period after cessation of stimulation. Additional input parameters were m = 2 and r = .25 times the standard deviation of the trial time series.[18] Entropy values were then averaged into blocks in the manner previously described for acquisition and retention. Lower entropy was interpreted as reduced postural system complexity, which is associated with impaired adaptive flexibility to environmental situations that challenge postural control.[20]

In order to demonstrate that calculation of SaEn was appropriate, the deterministic structure of the data was determined by a surrogation procedure.[21] This procedure produces a random data set with the same mean, variance, and power spectra as the original data set. Practically, surrogation randomly orders the sequence of the original data set in order to remove its temporal structure. If the original time series is deterministic, randomly ordering its sequence will remove this deterministic nature. A custom written program in Matlab (Mathworks, Natick, MA) was used to generate 20 surrogated data sets from each original time series. SaEn was calculated for each surrogated data set, and a 95% confidence interval was calculated from these values and compared to SaEn from the original data set. If original data demonstrated a deterministic structure, the SaEn will fall outside the 95% CI of the surrogated data.

Linear data (head COM position and COP CV) were analyzed using separate, 3x4x4 (Group x Stimulation x Time) mixed model analyses of variance (ANOVA) with repeated measures on the stimulation and time factors. In addition, SaEn during 6 seconds prestimulation and 6 seconds poststimulation recovery was analyzed using a 3x2x4 (Group x Stimulation x Time) mixed model ANOVA with repeated measures on

the stimulation and time factors. In the event of a significant finding in the omnibus F tests, post-hoc tests were performed using Bonferroni correction to correct for multiple comparisons of main effects between and within subjects. The initial level of significance for comparisons was set at 0.05. All statistical analyses were performed with SPSS 19 (IBM Inc; Armonk, NY,USA).

To establish the time to stabilization following sensory illusion, we adapted the method of Sozzi et al.[5] Briefly, we compared the coefficient of variation over one second of COP data prior to stimulation to coefficients of variation from 10 sequential 1-second epochs beginning at the cessation of GVS. Each time point was compared across groups and across acquisition and retention time period using a 3x4x11 ANOVA and post-hoc analyses with Bonferroni corrections for multiple comparisons. Post-hoc p values comparing pre- to sequential poststimulation time epochs were then plotted graphically for each group and each acquisition and retention point.[5] The first time the statistical difference between the pre- and poststimulation measure exceeded a 0.05 level of significance was assessed. Trend lines using linear, exponential, and power law functions were then constructed for the resultant graph to determine the best fitting estimate for COP CV stabilization time following the vestibular sensory illusion.

Results

Twenty-seven individuals with PD, 22 healthy elderly adults, and 17 healthy young adults were screened for inclusion in this study. Among individuals with PD who were excluded from the study, three had had surgery for their PD symptoms, four had a comorbid peripheral neuropathy, and eight had a Hoehn and Yahr score greater than III. Eleven elderly adults were excluded from participation due to recent orthopedic surgery

(n = 3), peripheral neuropathy (n = 5), and severe arthritis (n = 3). Two young adults were excluded from the study due to recent orthopedic injuries that affected their balance. Thirty-five participants completed testing. One individual in the PD group, two individuals in the HY group, and two individuals in the HE group did not have at least six complete seconds of data prestimulation and so were not included in the subsequent analyses. Therefore, analyses were performed on 33 participants. Participant characteristics are presented in Table 2.1. No subjects fell during any trial. As confirmation of the consistent effect of GVS, all participants demonstrated a significant and consistent rightward shift of head position immediately following GVS ($F = 2238.6$, $df = 1.06$, $p < .001$). This finding was not affected by repeated exposure to GVS, indicating that a consistent compensatory response was produced by the GVS-induced sensory illusion.

Influence of GVS on ML COP CV

There were no group x stimulation x time, or group x time interaction effects for COP CV. There was a significant group x stimulation interaction ($F = 4.3$, $df = 2.43$, $p = .016$; Figure 2.2). Post-hoc comparisons demonstrated that in the PD group, compared to COP CV at prestimulation ($\overline{x} = .009$, $CI_{95} = .007$-$.011$), there was significantly more COP CV at 1-3 seconds post (181.3% inc, $\overline{x}_{diff} = .017$, $CI_{95} = .011$-$.023$, $p < .001$) and 3-6 seconds post (30.1% inc, $\overline{x}_{diff} = .003$, $CI_{95} = .001$-$.005$, $p = .001$) stimulation. In contrast, compared to prestimulation in the HY ($\overline{x} = .006$, $CI_{95} = .004$-$.007$) and HE ($\overline{x} = .009$, $CI_{95} = .007$-$.011$) groups, COP CV only increased significantly 1-3 seconds post stimulation (HY = 135.4% inc, $\overline{x}_{diff} = .008$, $CI_{95} = .002$-$.013$, $p = .004$; HE = 105.1% inc, $\overline{x}_{diff} = .010$, $CI_{95} = .004$-$.016$, $p < .001$, respectively). This indicates that following stimulation,

Table 2.1: Participant Characteristics (N=34)

	HY (N=14) $\overline{x}$ (95% CI)	PD (N=11) $\overline{x}$ (95% CI)	HE (N=9) $\overline{x}$ (95% CI)
Age (yrs)	25.5 (24.2-26.8)	70.6 (64.6-76.7)	63.8 (55.2-72.3)
Hgt(cm)	171.6 (165.1-178.3)	173.7 (168.5-178.9)	172.7 (169.2-176.1)
Wgt(kg)	73.8 (61.3-86.3)	81.9 (75.5-88.4)	85.8 (71.9-99.7)
FGA	--- NA ---	23.9 (21.4-26.4)	27.9 (25.9-29.9)
UPDRS	--- NA ---	18.8 (11.9-24.5)	--- NA ---

FGA – Functional Gait Assessment

UPDRS – Motor Subcomponent of Movement Disorders Society Unified Parkinson Disease Rating Scale

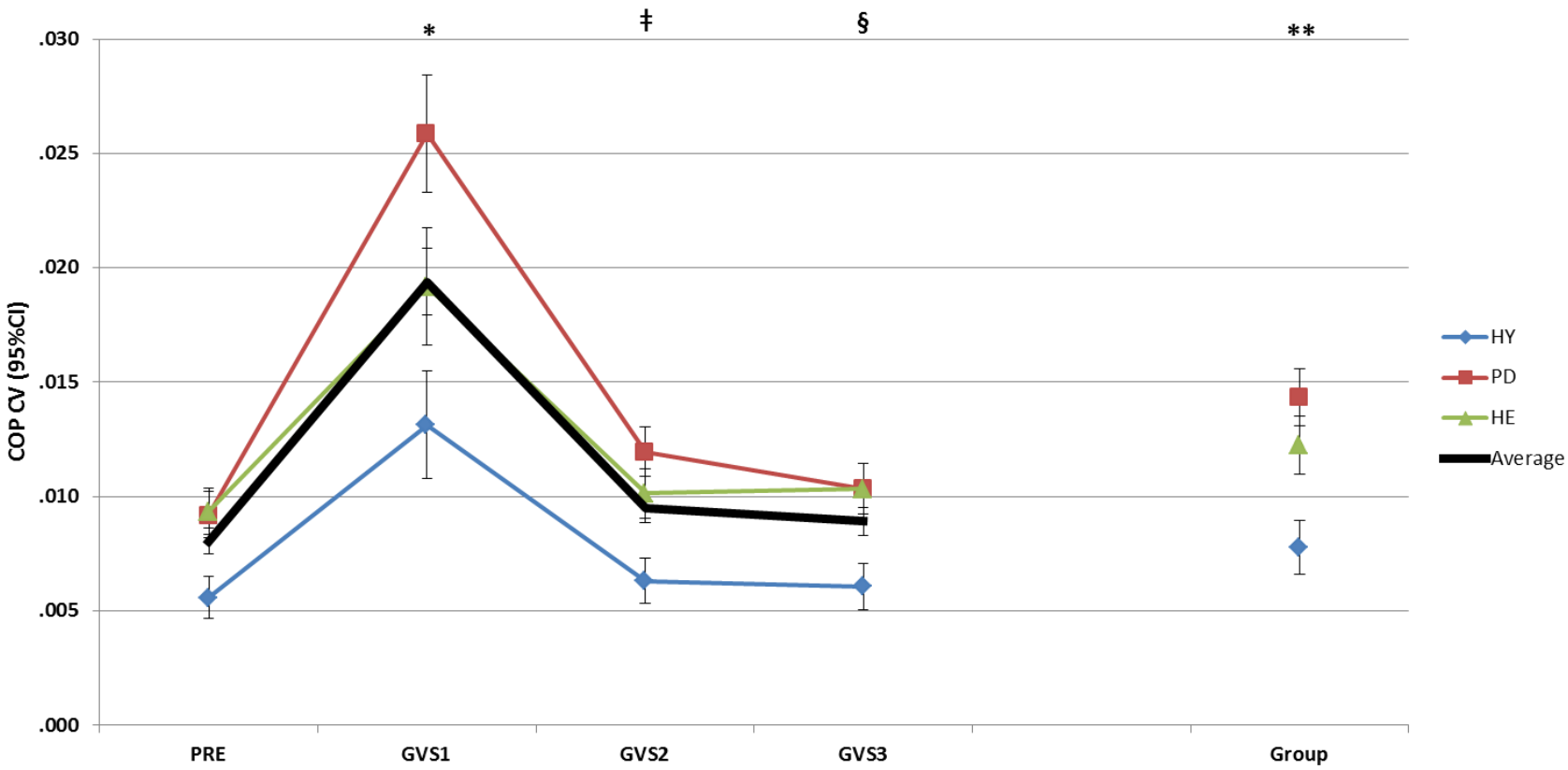

Figure 2.2: Average Within Trial Group COP CV at Prestimulation and Poststimulation; Overall Group COP CV Averages
* Significant COP CV increase overall and all groups; ǂ significant COP CV increase overall and PD; § significant COP CV increase overall; **Significant COP CV difference between groups (significance $p < 0.05$ all comparisons)

individuals with PD took longer than controls to stabilize their COP. There was a related significant main effect of stimulation on COP CV ($F = 75.1$, $df = 1.22$, $p < .001$; Figure 2.2 black line). Post-hoc comparisons demonstrated that compared to prestimulation ($\overline{x} = .008$, $CI_{95} = .007\text{-}.009$), COP CV increased at 1-3 seconds (141.2% inc, $\overline{x}_{diff} = .011$, $CI_{95} = .008\text{-}.015$, $p < .001$), 3-6 seconds (17.8% inc, $\overline{x}_{diff} = .001$, $CI_{95} = .0004\text{-}.002$, $p = .002$), and 6-9 seconds (10.8% inc, $\overline{x}_{diff} = .001$, $CI_{95} = .0005\text{-}.002$, $p < .001$) post stimulation. This indicates that on average, while GVS decreased COP stability overall, stability improved as the trial progressed.

There was a significant time x stimulation interaction ($F = 7.9$, $df = 4.81$, $p < .001$; Figure 2.3, black line). Post-hoc comparisons demonstrated that prestimulation COP CV during early acquisition ($\overline{x} = .008$, $CI_{95} = .007\text{-}.009$) was lower than at 1-3 seconds post (203.4% inc, $\overline{x}_{diff} = .016$, $CI_{95} = .011\text{-}.022$, $p < .001$) and 3-6 seconds post (27.4% inc, $\overline{x}_{diff} = .002$, $CI_{95} = .0005\text{-}.004$, $p = .017$) stimulation. In contrast, at midacquisition, late acquisition, and retention, prestimulation COP CV (MID: $\overline{x} = .008$, $CI_{95} = .007\text{-}.010$; LATE: $\overline{x} = .008$, $CI_{95} = .007\text{-}.010$; RET: $\overline{x} = .008$, $CI_{95} = .006\text{-}.009$) was lower than COP CV at 1-3 seconds poststimulation only (MID: 142.9% inc, $\overline{x}_{diff} = .012$, $CI_{95} = .007\text{-}.017$, $p < .001$; LATE: 110.5% inc, $\overline{x}_{diff} = .009$, $CI_{95} = .005\text{-}.014$, $p < .001$; RET: 105.9% inc, $\overline{x}_{diff} = .008$, $CI_{95} = .005\text{-}.011$, $p < .001$, respectively). Additionally, COP CV significantly decreased from early to late acquisition (25% dec, $\overline{x}_{diff} = .007$, $CI_{95} = .002\text{-}.012$, $p = .004$) and early acquisition to retention (37.5% dec, $\overline{x}_{diff} = .009$, $CI_{95} = .005\text{-}.014$, $p < .001$) at 1-3 seconds poststimulation, while significant changes were not found at other pre- or poststimulation points across acquisition and retention. This indicates that all subjects developed better control of COP position

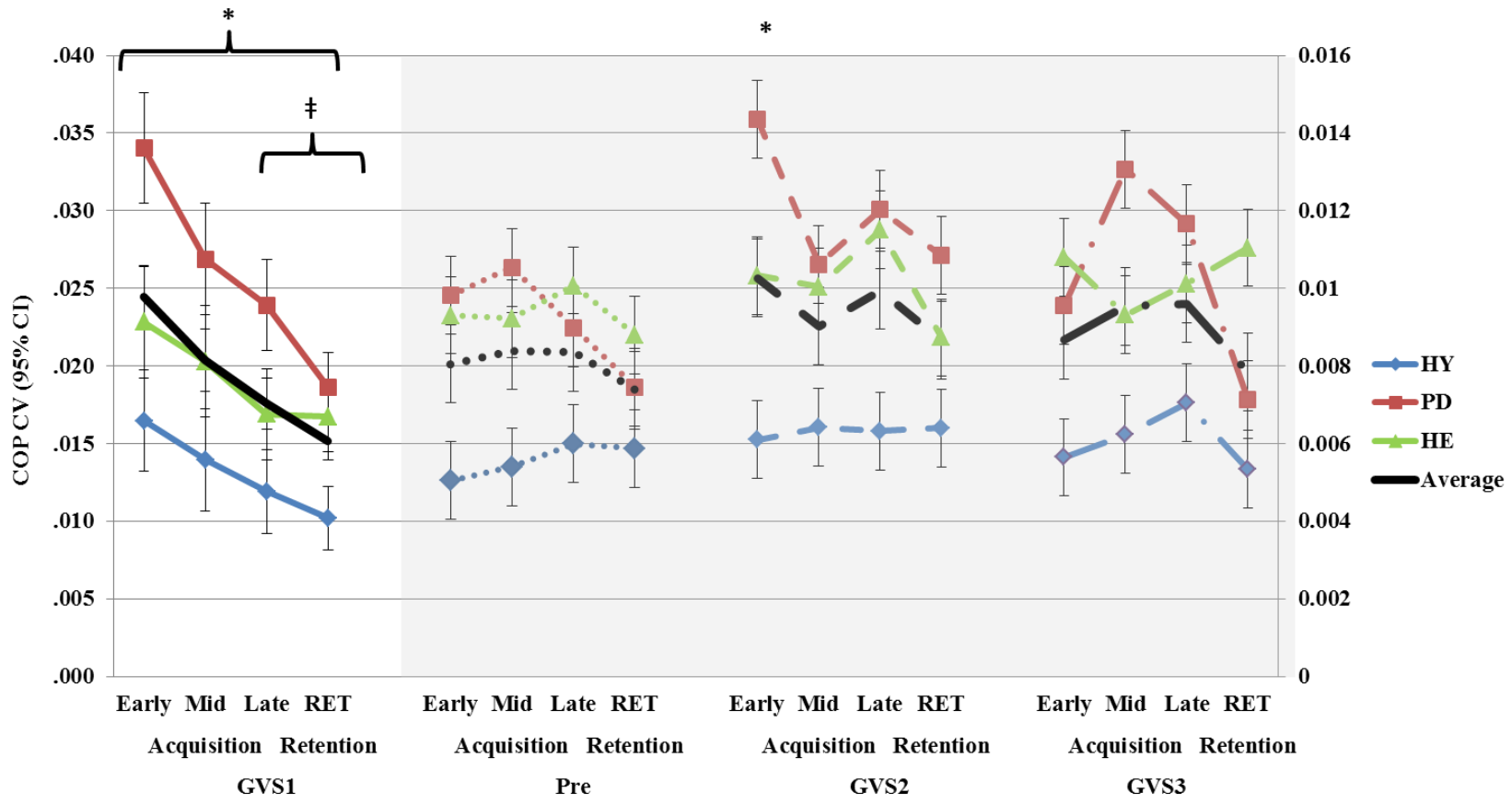

Figure 2.3: Average Between Trial Group COP CV at Prestimulation, Acquisition, and Retention
* Significant overall COP CV increase compared to Pre; ǂ significant COP CV decrease overall compared to Early (significance $p < 0.05$ all comparisons); Note different scale magnitude for variables in gray area

changes with repeated exposure to GVS by stabilizing their COP position within 3 seconds at later acquisition and retention time points and by decreasing their COP CV during that 3 second period across acquisition and retention.

There was a significant between-group effect on ML COP position CV (F = 7.8, df = 2, p = .002; Figure 2.2). Post-hoc comparisons demonstrated that on average, the HY group ($\overline{x}$ = .008, CI_{95} = .005-.010) had significantly less COP position CV than the PD group (84.5% inc, $\overline{x}_{diff}$ = .007%, CI_{95} = .002-.011, p = .002) or the HE group (57.6% inc, $\overline{x}_{diff}$ = .004, CI_{95} = .001-.009, p = .041). This indicates that the HY group was better able to control changes in COP position following GVS than either older adults or individuals with PD.

There was a significant time effect on COP CV (F = 8.6, df = 2.52, p < .001; Figure 2.4, black line). Post-hoc comparisons demonstrated that COP CV at early acquisition ($\overline{x}$ = .013, CI_{95} = .011-.015) was similar to mid acquisition (8% dec, $\overline{x}_{diff}$ = .001, CI_{95} = -.001-.003, p > .05) and late acquisition (11.5% dec, $\overline{x}_{diff}$ = .001, CI_{95} = .00-.003, p > .05), but significantly higher than retention (24% dec, $\overline{x}_{diff}$ = .003, CI_{95} = .001-.005, p < .001). This indicates that some motor learning occurred following consolidation allowing an improved ability to stabilize changes in COP position following GVS, irrespective of group.

Influence of GVS on ML COP SaEn

Results comparing SaEn to the 95% CI of SaEn from surrogated data demonstrated that our data had a deterministic structure. With respect to our COP data, prior to stimulation, SaEn in the HY group ranged from .356-.395 across acquisition and retention time points. Entropy was lower in the HE and PD groups prior to stimulation

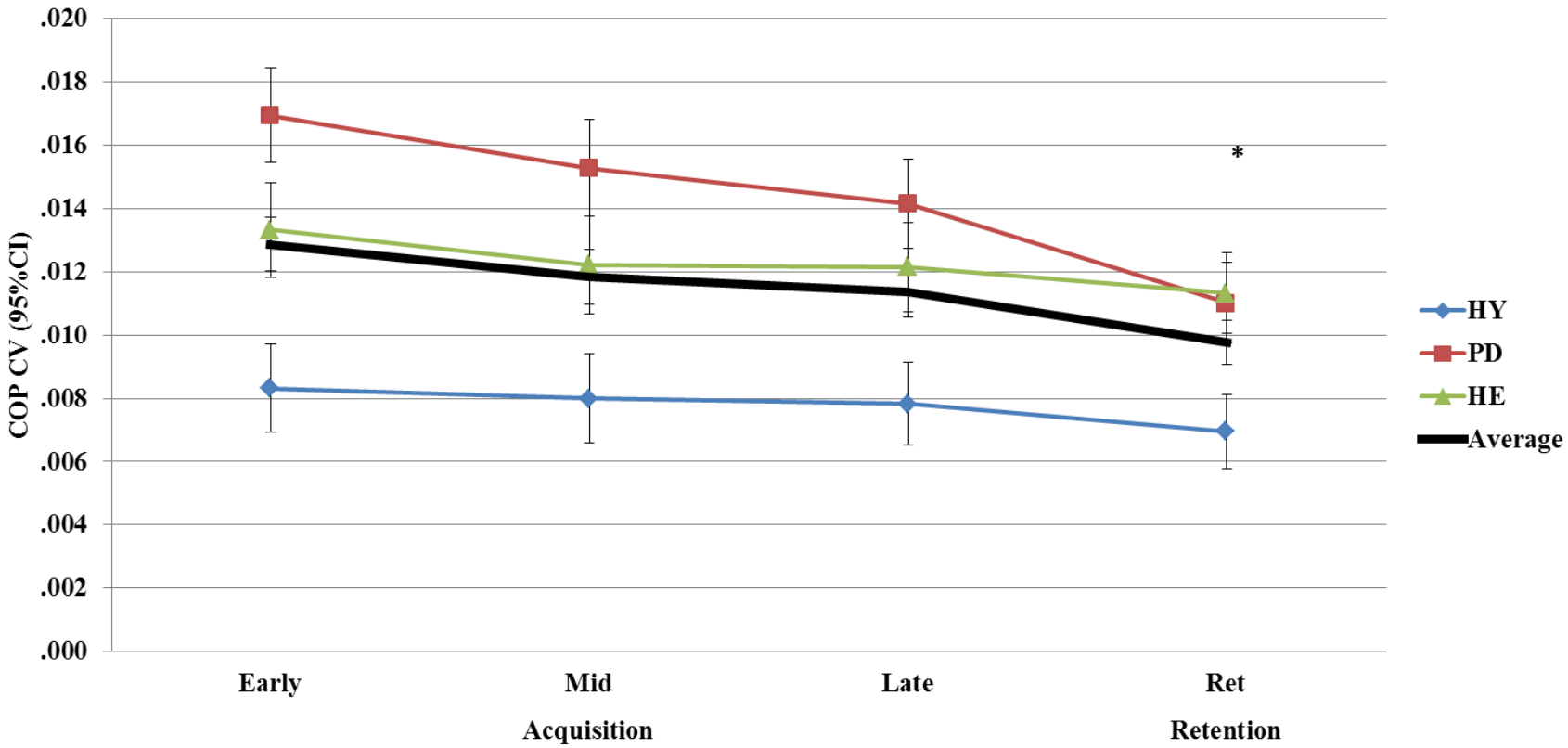

Figure 2.4: Average Between Trial COP CV Changes at Prestimulation, Acquisition, and Retention
* Significant overall COP CV decrease compared to Early Acquisition (significance $p < 0.05$ all comparisons)

during acquisition and retention, ranging from .106-.136 and .090-.130, respectively. Entropy decreased in all groups poststimulation across acquisition and retention, ranging from .138-.296 in the HY group, .078-.097 in the HE group, and .054-.071 in the PD group.

There was a significant group x stimulation x time interaction effect for ML COP SaEn ($F = 2.3$, $df = 3.82$, $p = .043$; Figure 2.5). Post-hoc comparisons demonstrated that SaEn between the PD and HE groups did not differ at any time point before or after stimulation ($p > 0.05$, all comparisons). Entropy in the HY group was significantly higher than in the PD group ($p \leq .002$ prestimulation, $p \leq .001$ poststimulation, all comparisons) and HE group ($p \leq .002$ prestimulation, $p \leq .041$, all comparisons) throughout acquisition and retention. Additionally, post-hoc comparisons demonstrated that prior to stimulation, SaEn was similar across acquisition and retention in the PD group ($p > 0.05$, all comparisons) and each control group ($p > 0.05$, all comparisons). Following stimulation, SaEn was similar across acquisition and retention in the PD group ($p > 0.05$, all comparisons) and HE group ($p > 0.05$, all comparisons), but the HY group showed a significant increase in SaEn at retention ($\overline{x} = .296$, $CI_{95} = .224$-$.367$) compared to early ($\overline{x} = .138$, $CI_{95} = .111$-$.164$), mid ($\overline{x} = .168$, $CI_{95} = .134$-$.203$) and late ($\overline{x} = .158$, $CI_{95} = .128$-$.188$) acquisition. There was also a significant main group effect for ML COP Entropy ($F = 24.6$, $df = 2$, $p < .001$; Figure 2.5), which was explained by the interaction, in that the HY group had significantly higher entropy ($\overline{x} = .281$, $CI_{95} = .239$-$.323$) than the PD ($\overline{x}_{diff} = .197$, $CI_{95} = .118$-$.276$, $p < .001$) or HE groups ($\overline{x}_{diff} = .179$, $CI_{95} = .095$-$.262$, $p < .001$), while there was no difference between the latter groups.

There was no stimulation x time interaction effect. There was a significant group

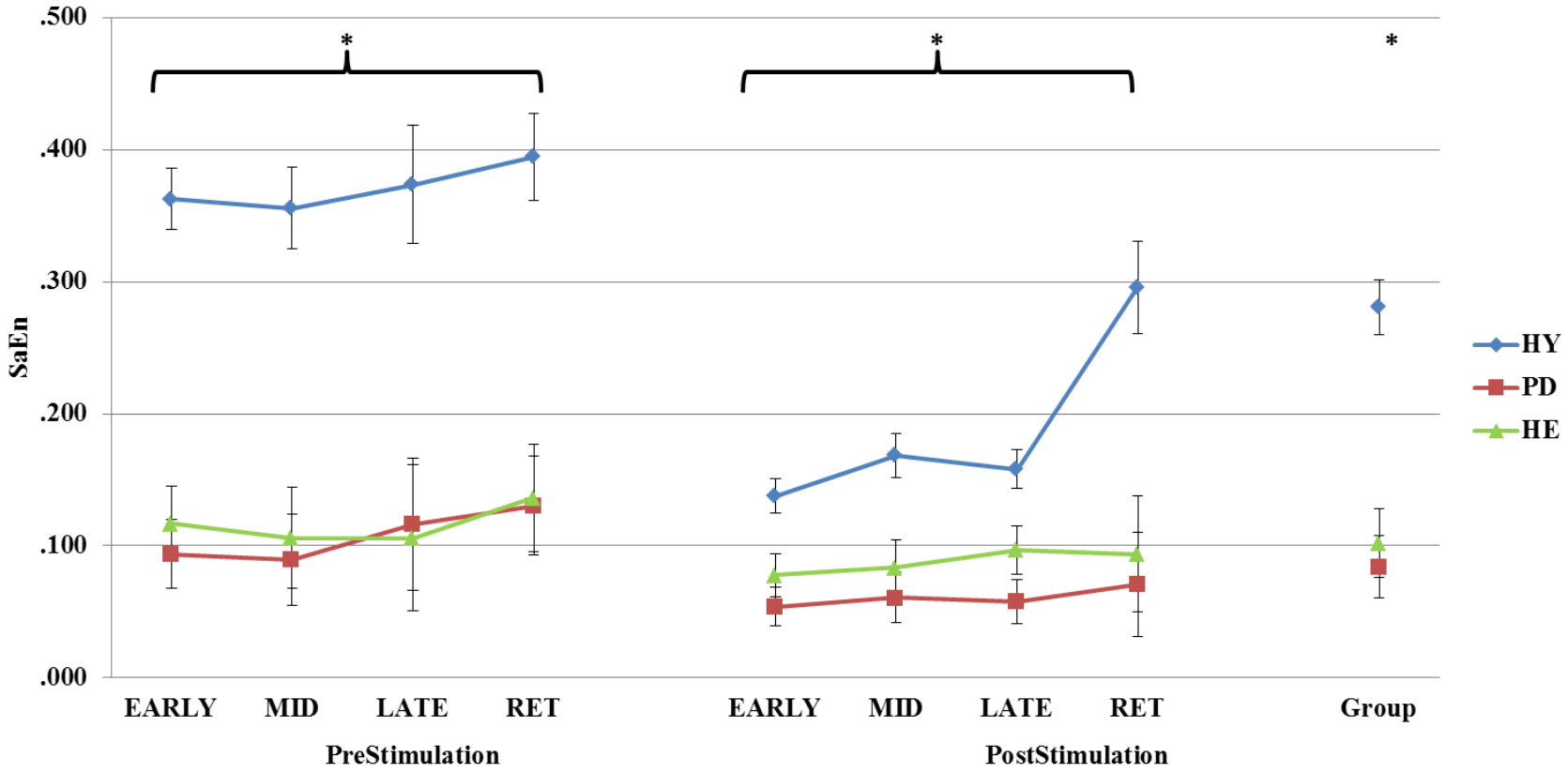

Figure 2.5: Average Between Trial Group SaEn at Prestimulation and Poststimulation; Overall Group COP CV Averages
* Significant difference in SaEn between HY and PD / HE groups; ǂ significant increase in SaEn in HY group at Ret; (significance $p < 0.05$ all comparisons)

x stimulation interaction (F = 13.7, df = 2, p < .001; Figure 2.6). Post-hoc comparisons demonstrated that compared to prestimulation in the HY group ($\overline{x}$ = .372, CI_{95} = .313-.431), there was a significant reduction in SaEn after stimulation ($\overline{x}_{diff}$ = .182, CI_{95} = .139-.225, p < .001). There was a trend toward decreased SaEn in the HE and PD groups poststimulation, but these changes failed to reach statistical significance. There was also a significant main effect of stimulation on ML COP SaEn (F = 38.8, df = 1, p < .001). Post-hoc comparisons demonstrated that SaEn significantly decreased pre- ($\overline{x}$ = .198, CI_{95} = .160-.237) to poststimulation ($\overline{x}_{diff}$ = .086, CI_{95} = .058-.114, p < .001). This difference is attributable to the large reduction in entropy in the HY group pre- to poststimulation identified in the group x stimulation interaction.

The group x time omnibus test failed to demonstrate significance (F=1.6, df =4.04, p > 0.05; Figure 2.7). However, post-hoc analysis did demonstrate that there was a significant increase in SaEn between each acquisition time point and retention ($\overline{x}_{diff}$ range = .079-.095, p range = .010-.002) in the HY group, but not in the PD or HE groups. Additionally, there was a significant main effect of time for ML COP SaEn (F = 5.2, df = 2.02, p = .008; Figure 2.7). Post-hoc comparisons demonstrated that entropy at early acquisition ($\overline{x}$ = .140, CI_{95} = .119-.162) and mid acquisition ($\overline{x}$ = .144, CI_{95} = .117-.171) was significantly lower than at retention ($\overline{x}$ = .187, CI_{95} = .145-.229, p ≤ .017).

Time to Stabilization During Postural Recovery

Group comparisons did not differ from one another, nor did comparisons across acquisition and retention. Therefore, an average result was used to graph statistical differences from pre- to poststimulation. We found that the our data were best represented by a power law function estimate for the time COP CV stabilized following

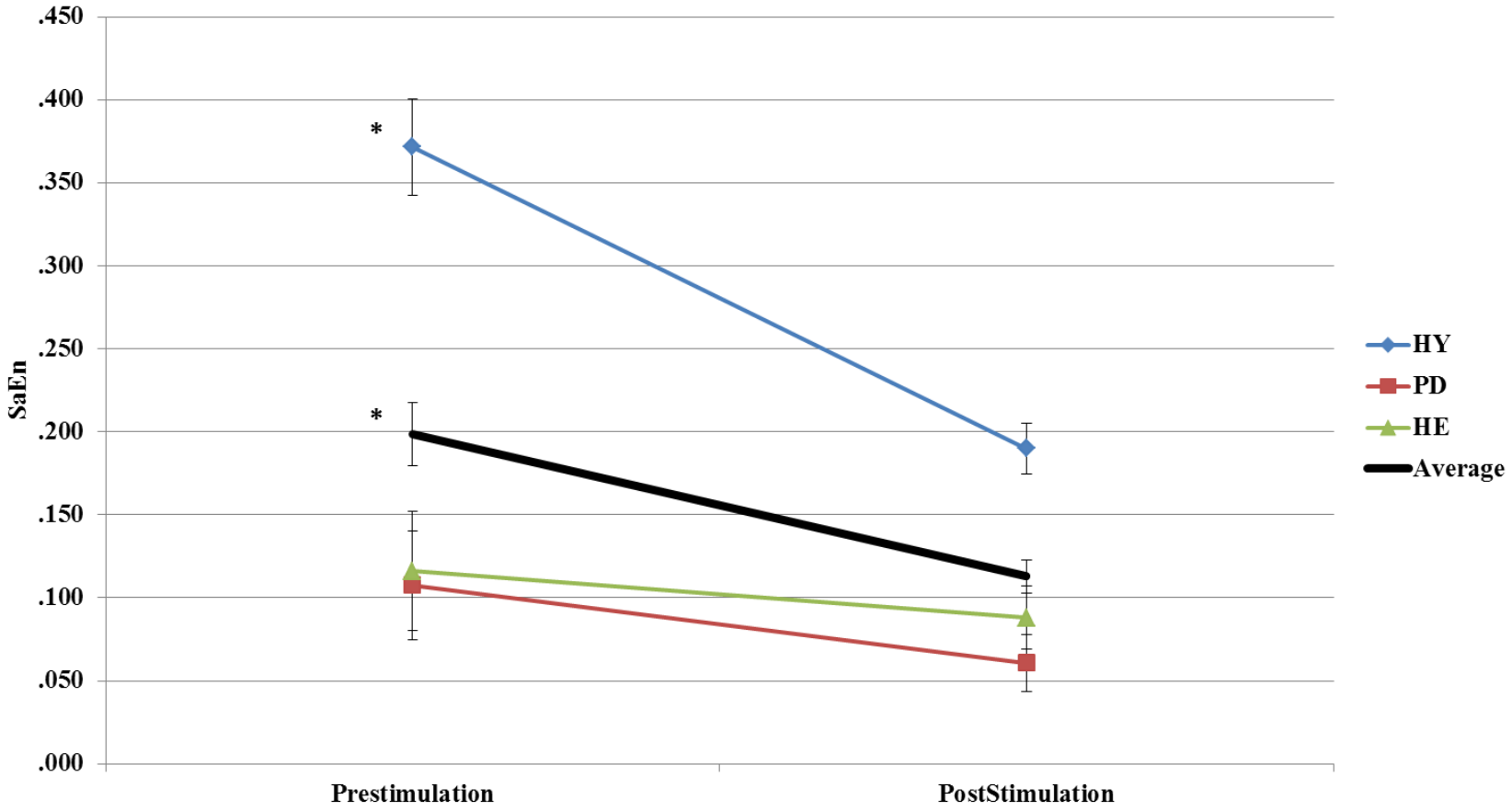

Figure 2.6: Average Within Trial Group SaEn at Prestimulation and Poststimulation
* Significant decrease in SaEn overall and in HY (significance $p < 0.05$ all comparisons)

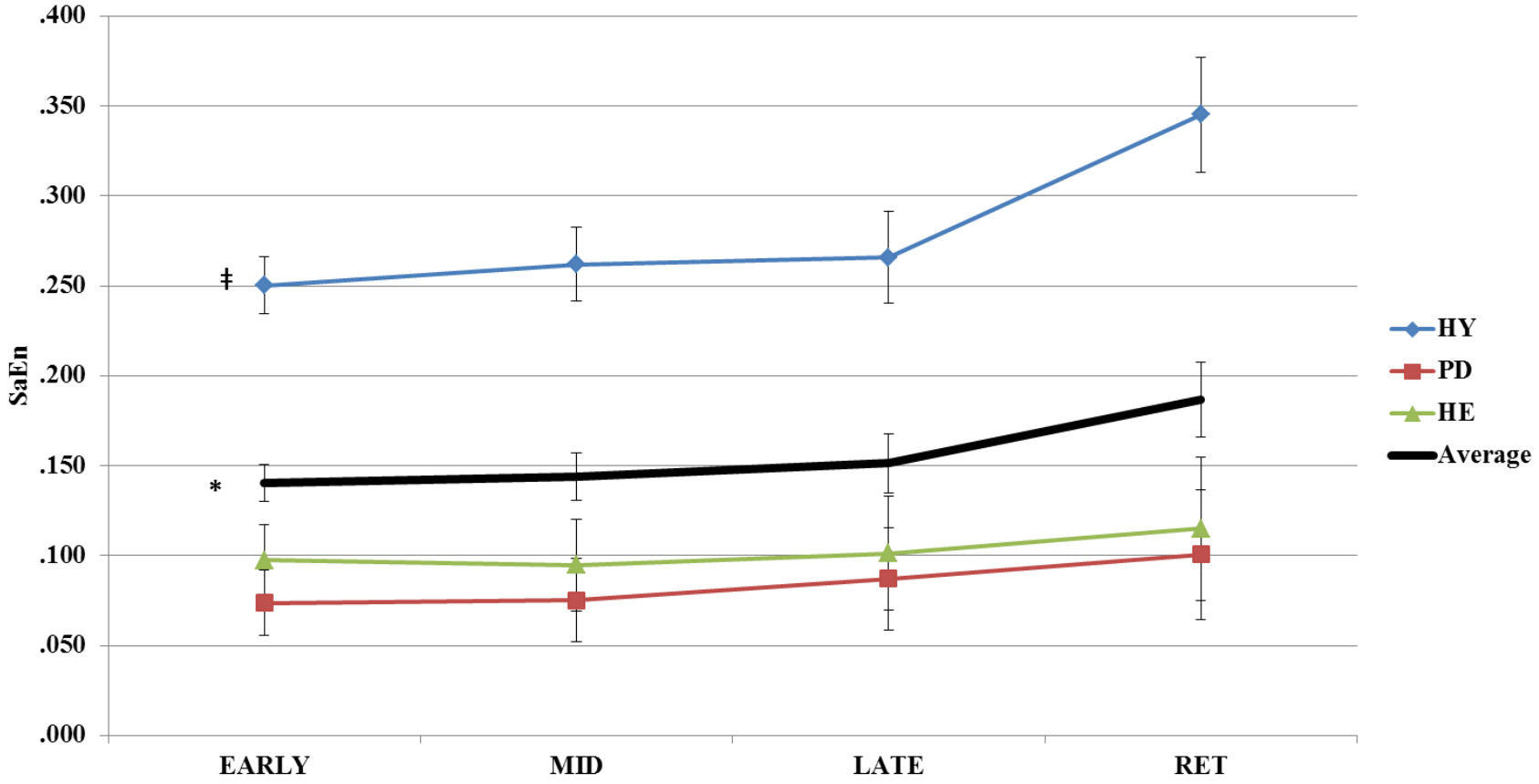

Figure 2.7: Average Between Trial SaEn at Prestimulation, Acquisition, and Retention
* Significant overall increase in SaEn at retention compared to Early Acquisition; ǂ post-hoc significant increase in SaEn for HY group (significance $p < 0.05$ all comparisons)

GVS (Figure 2.8), which showed that COP CV decreased to prestimulation levels within 3.5 seconds after cessation of stimulation ($R^2 = 0.85$).

Discussion

The current study sought to determine whether Parkinson disease or age would differentially affect acute postural recovery to vestibular sensory illusion and whether repeated exposure to a vestibular sensory illusion would differentially affect adaptation of postural control in these groups compared to healthy controls. We also sought to determine the time course of postural recovery following a vestibular sensory across groups. We hypothesized that individuals with Parkinson disease would demonstrate an impaired postural recovery response to acute GVS exposure relative to neurologically healthy controls and that both individuals with PD, and older healthy adults would demonstrate less robust adaptive responses to repeated GVS exposure than healthy young adults. We further hypothesized that postural recovery following GVS would occur in a predictable time course regardless of age or PD. Our results supported our overall hypotheses. Individuals with PD had a delayed ability to stabilize COP following acute exposure to GVS; the PD and HE groups demonstrated less robust adaptive responses to repeated GVS exposure, and the estimated time course for postural recovery following a sensory illusion was predictable and consistent across groups.

Acute Influence of GVS on Postural Recovery

All subjects had a marked increase in COP CV 1-3 seconds after GVS exposure, though individuals with PD had a more robust response (Figure 2.2). Additionally, though COP CV in the PD group decreased in a similar manner as controls at 3-6 seconds

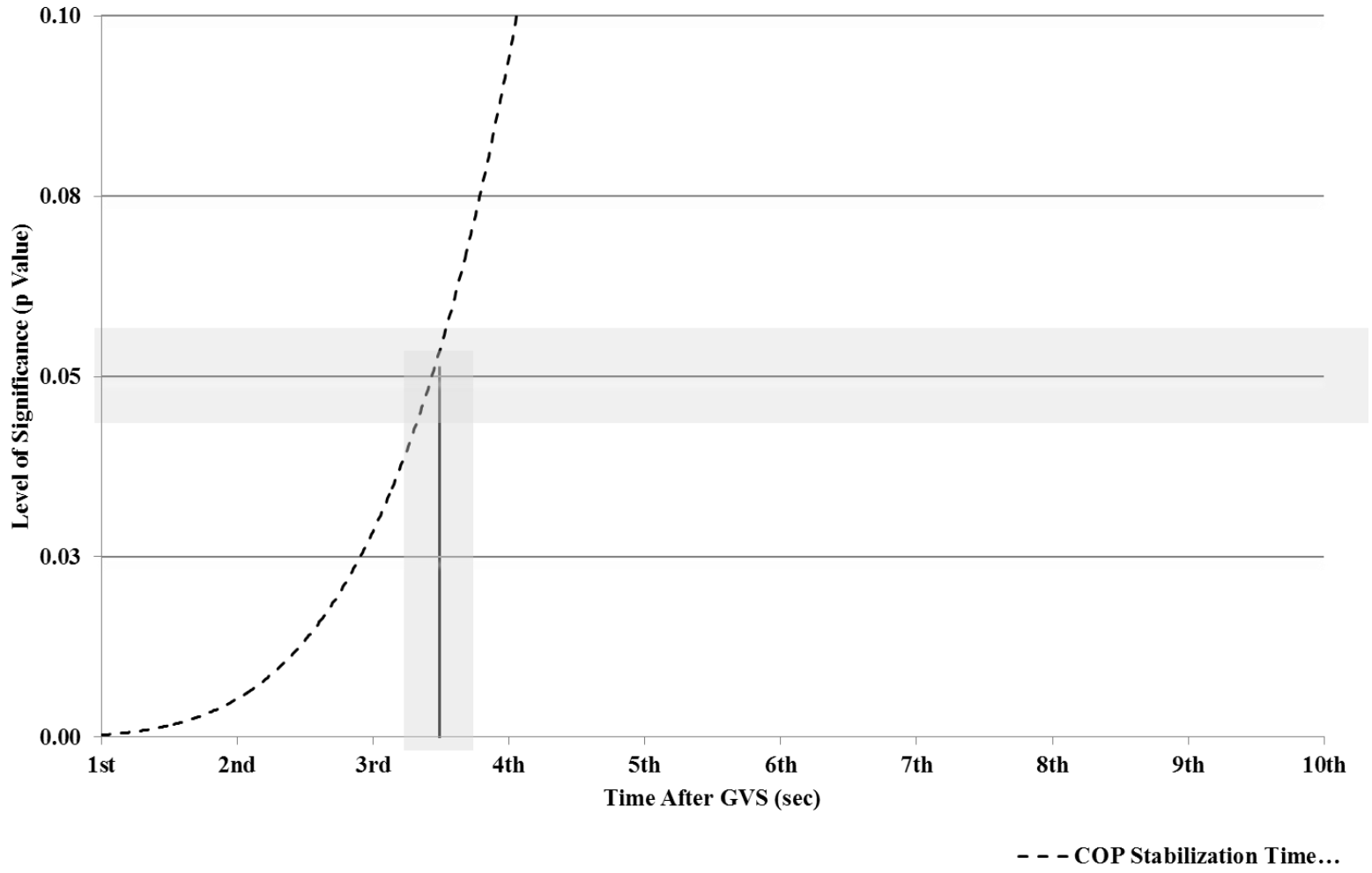

Figure 2.8: Power Law Function Curve Fitting for Postural Recovery Time

poststimulation, it did not decrease to the same relative magnitude, indicating that PD subjects did not stabilize as well as controls at this point. These findings indicate that individuals with PD have a diminished capacity to stabilize their COP acutely following sensory illusion. Brown et al.[2] drew a similar conclusion when studying postural responses following removal of vision. The greater degree of difficulty in stabilizing COP acutely in individuals with PD may be related to a decrease in postural system complexity in these individuals. We found that both individuals with PD and older control subjects had significantly lower SaEn values than did healthy controls (Figure 2.5). This demonstrates that postural control diminishes with age in such a way that its temporal structure during quiet stance becomes more regular. Increased regularity has previously been associated with a constraint on the degrees of freedom of movement and is likely indicative of physiologic changes in motor output that decrease movement complexity.[15,22] Paradoxically, increased regularity may result in a reduced capacity to adapt to new environmental or sensory threats. Harbourne et al.[15] have posited the idea that normal development of postural control is associated with an initial increase (lower entropy) and subsequent decrease (higher entropy) in regularity, allowing the individual to temporarily impose a state of greater stability in the face of novel postural experiences as they learn to control movement in a new environment. Once the basics of movement in the new environment are mastered, the regularity of system output gradually decreases (complexity increases) toward an optimal level, allowing a more rich, varied, and adaptable postural experience. We observed a small and nonsignificant decrease in SaEn from pre- to poststimulation in PD and older adults, while vestibular sensory illusion led to a large average decrease in SaEn among healthy young adults (Figure 2.6). This may

reflect a difference in the adaptive nature of the mature central nervous system to sensory illusion with aging. We hypothesize that the young adults were able to adapt their postural control behavior to the novel sensory illusion, demonstrating an exploratory strategy in order to learn to adapt to the new threat, while complexity of system output in the older groups did not appreciably change in response to the GVS. The lack of change may have occurred because of the already lower complexity of motor system output in older adults which could impair the ability of the central nervous system to attempt to further increase regularity as new postural strategies are explored. This in turn would compromise subsequent postural control performance changes and adaptation. We acknowledge that this interpretation is speculative and in need of further research.

Influence of Repeated Exposure to GVS on Postural Adaptation

There was a general improvement in COP CV across all subjects following early acquisition as evidenced by the 28% decrease in COP CV at late acquisition and 37% decrease at retention during the first 3 seconds of postural recovery (Figure 2.3) and the overall 24% decrease in COP CV at retention (Figure 2.3). Taken together, these data demonstrate a general improvement in postural control with repeated GVS exposure. Though we did not find significant group by time interactions for COP CV, it is informative to consider the differences in these patterns (Figure 2.3) as it provides clinically meaningful insight. Poststimulation COP CV was lower in the HY group than the older groups across the majority of acquisition and retention comparison (Figure 2.3). More importantly, COP CV at retention in the 1-3 seconds poststimulation was similar to prestimulation levels in this group (Figure 2.3). This indicates that not only did the HY group have better postural control following GVS overall, they had a more robust

adaptive response at retention to repeated GVS exposure. The PD group had the greatest decrease in COP CV magnitude 1-3 seconds poststimulation across time, and their average CV was approximately equal to their healthy age-matched counterparts at retention, which indicates that individuals with mild to moderate PD have the ability to improve postural control during recovery from a sensory illusion to a degree commensurate with healthy older adults. However, neither of these groups demonstrated a tendency to reduce COP CV to prestimulation levels, which suggests that although they demonstrated some improvement, age was likely to have limited the ability to adapt to repeated exposure to a sensory illusion in a manner commensurate with healthy younger adults over the same time course.

We saw a similar overall improvement in postural control across subjects at retention through the increase in SaEn (Figure 2.7), though closer inspection demonstrates that this change was primarily the result of two factors. First, there was a trend in all groups to marginally increase SaEn between early acquisition and retention during unperturbed quiet stance (Figure 2.5), which may be attributable to individuals improving their ability to stand with their base of support constrained.[23] Second, and more importantly, at poststimulation the HY group demonstrated a significant and substantial increase in system complexity between early acquisition and retention, while SaEn in the older groups was unchanged (Figure 2.5).

The combination of the decrease in COP CV to prestimulation levels and the significant increase in SaEn at retention in the HY group suggest that these individuals learned to adapt their postural strategy to the sensory illusion in a short time period, more robustly than older adults. One potential explanation was the use of a more responsive

sensory reweighting ability in which conflicting sensory information was successfully suppressed. Our findings here are not surprising; previous research has shown that young healthy adults are able to adapt their postural responses during a single session of prolonged, repeated GVS and maintain improvement over a 6-month washout period.[10] Similar results have been reported when reweighting visual[24,25] and proprioceptive[26] inputs.

Neither the PD nor HE groups showed improvements in postural complexity nor did they demonstrate clinically meaningful changes (eg, reducing COP CV to prestimulation levels) in COP CV with repeated exposure to the vestibular illusion either during acquisition or retention testing following a 48-hour period allowing for consolidation. The lack of adaptability in these groups compared to young adults may be attributable to decreased sensorimotor learning efficiency for these subjects. Adaptive reweighting of sensory stimuli to visual illusion has been shown to be intact, but delayed in older healthy individuals.[24,25] Similarly, adaptation to change in visual condition during a single session has been shown to be delayed in individuals with PD while standing on a continuously moving platform compared to age-matched controls.[4] Both of the older groups showed similar decreases in COP CV across time, and it is possible that continued exposure to GVS would have demonstrated an adaptive response of the same relative magnitude shown in young adults. Despite our observation that GVS produced a consistent postural recovery response across subjects, it is possible that the sensory illusion presented was inadequate to drive a more robust change in older individuals. Older healthy individuals and those with PD have a greater reliance on visual information for maintenance of postural stability.[27,28] In individuals with PD,

impairment in processing of proprioceptive information may even serve to enhance reliance on visual information.[29] Given the bias of these individuals toward visual reliance for postural control, they may have a diminished capacity to adapt to other sensory illusions when vision is present. This would account for both the larger amount of COP CV and the lower system complexity we observed in these groups. Our findings support a rationale to ensure that an adequate dosage of sensory perturbations are provided within balance training programs that wish to utilize sensory reweighting components. Specifically, our results demonstrate that older adults and those with PD respond similarly to healthy young adults with respect to acute sensory perturbation, but have dissimilar adaptive responses. This suggests that the former groups may require longer training periods with single or multisensory manipulation in order to modify their postural control in such a way to mitigate their fall risk.

We found that a nonlinear measure (SaEn) was more responsive to group differences in adaptation to sensory illusion than a traditional measure (COP CV) of postural control as indicated by the significant shift in SaEn acutely and a subsequent significant reversal following repeated exposure and a period of consolidation. While this was the first study to evaluate adaptive changes in postural system complexity following repeated exposure to a vestibular sensory illusion, our findings support previous research that has shown that nonlinear measures provide a complementary evaluation of postural control and potentially provides greater insight into subtle nuances of its behavior.[30-33]

Postural Recovery Time to Stabilization

The estimated time to stabilization following GVS fit well with our empirical data. The trend line of the power law function estimated a stabilization time of 3.5

seconds following GVS. From our experimental results comparing 3-second intervals of COP CV following GVS across acquisition and retention, we found that COP CV was only significantly increased beyond 3 seconds during early acquisition when stimulation was most novel. Sozzi et al.[5] found that the COP stabilized within 1-2 seconds following changes in visual condition. Differences in our results may be due to methodological variations as we studied a vestibular rather than visual illusion and measured COP CV, rather than position. However, differences may also be because the vestibular sensory illusion used here produces a perceived change in head on body orientation, which may be more novel and therefore more difficult to regulate than a change in visual condition.

Limitations and Future Directions

While our results demonstrated the limitations of persons with PD and HE to adapt to sensory illusions, they should be interpreted with caution. First, the current work may have been limited by the low amplitude, short duration vestibular stimulation applied in producing a robust postural disturbance. Head COM and COP data, however, show that a predictable and reproducible change in equilibrium position occurred following stimulation across all time points. Additionally, it was our intent to study adaptation of recovery from a transient sensory illusion, rather than produce an adaptive postural response to a sustained illusion as has previously been done.[10,34] Future research should evaluate the effects of longer training periods of transient and sustained GVS on postural recovery responses after stimulation cessation in older and neurologically impaired populations to determine optimal adaptation transfer.

Allowing subjects to maintain a normal complement of other sensory inputs responsible for postural stability may also have limited our findings. However, since the

effects of vestibular sensory illusions in older and neurologically impaired populations have not been extensively studied, we felt it was appropriate to only evaluate a single modality perturbation at this time. Future research should compare single and multiple simultaneous sensory illusions to broaden the understanding of postural adaptation potential and constraints in these populations.

Finally, age matching was imperfect in the current study, which potentially limited our ability to discern between age-related and PD-related differences in postural control following acute or repeated GVS application. In order to mitigate this weakness in our study, we conducted separate ANCOVAs for each variable of interest, comparing individuals with PD and healthy elders using age as a covariate. Results of these analyses did not differ from results of similarly conducted ANOVAs comparing these groups. Future research should seek to confirm our findings in a larger cohort of individuals with PD and healthy elders using a tighter restriction on age-matching.

Conclusion

Acute exposure to a vestibular sensory illusion produced a similar and reproducible postural disturbance in individuals with PD and young and older healthy controls. Center of Pressure CV decreased over time with repeated exposure to GVS, but only reached a clinically important level in young adults. Sample entropy, an indicator of postural control system complexity, showed a marked acute reduction followed by an adaptive increase with training in young adults, while both older age groups demonstrated lower overall SaEn without acute or adaptive responses to GVS. Longer training intervals may be needed to produce salient and robust adaptive sensory reweighting responses in older adults.

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CHAPTER 3

INFLUENCE OF GALVANIC VESTIBULAR STIMULATION ON ACUTE AND ADAPTIVE RESPONSES OF AN ANTICIPATORY POSTURAL TASK: EFFECTS OF PARKINSON DISEASE AND AGE

Abstract

The ability of the elderly or individuals with Parkinson disease (PD) to reweight sensory stimuli to optimize postural control during anticipatory postural tasks is understudied, but a relevant factor in mitigating fall risk in these populations. The purpose of this study was to determine whether postural responses associated with an anticipatory postural task are differentially affected by novel or repeated exposure to GVS among elderly individuals or those with Parkinson disease (PD). Individuals with PD demonstrated impaired motor planning, a small but potentially meaningful aberration in postural preparation, and decreased postural stability following acute exposure to GVS, while healthy controls demonstrated an ability to effectively suppress GVS exposure acutely. Individuals with PD learned to suppress the sensory illusion following repeated exposure to GVS, as evidenced by improved motor planning, restoration of normal postural preparation, and improved postural stability at later acquisition and retention time points. Taken together, these findings indicate that the ability to reweight sensory stimuli to improve postural control is impaired, but present in individuals with

PD. Additionally, our findings suggest that the healthy nervous system rapidly suppresses vestibular illusions when performing a voluntary postural task that requires a planned change or reduction in the base of support (BOS). In this context the central nervous system (CNS) may rely more heavily on somatosensory or visual information to meet the objectives of the task.

Introduction

Postural instability is a hallmark feature of Parkinson disease (PD), particularly as the disease progresses. The etiology of postural instability in the disease is multifactorial, but is related to rigidity, bradykinesia, muscle weakness, and impairment of sensory integration.[1-4] Timely and accurate integration of sensory information is necessary to produce a context appropriate motor response and optimize postural control in a changing physical environment.[5] When sensory information is in conflict, such as when observing the horizon while standing on the bow of a boat being rocked by waves, the central nervous system functions to downregulate inaccurate sensory cues and upregulate accurate cues in order to maintain postural equilibrium.[6] Recent studies have demonstrated that individuals with PD have centrally mediated proprioceptive deficits.[2] These deficits may result in an overreliance on remaining sensory modalities in an attempt to produce appropriate motor responses to perturbation.[7,8]

Postural responses in PD to somatosensory and visual sensory conflict are well defined.[9-13] However, the influence of vestibular conflict on postural control in this population is less apparent. Sensory illusions of the vestibular system are commonly evoked in research settings using galvanic vestibular stimulation (GVS), which uses a low amplitude, transcutaneous electrical current to stimulate vestibular nerve afferents

and produce the illusion of a head on body translation.[14] Individuals with PD and controls have similar acute responses to GVS during quiet stance.[15] However, healthy individuals are able to reweight sensory input with repeated exposure to GVS during quiet stance in order to restore postural equilibrium,[16] and it is currently not known whether individuals with PD display similar adaptive capabilities. Additionally, the context in which the sensory conflict is evoked may affect both the acute and adaptive responses to the sensory illusion. Previous research has shown that the timing of GVS during step initiation differentially affects subsequent postural responses in healthy adults.[17] Postural responses to a vestibular sensory illusion during a more difficult anticipatory postural task, however, have not previously been reported. Clearly, in order to better understand how individuals with PD respond to sensory illusions, it is important to evaluate the spectrum of sensory systems involved in postural stability and determine the magnitude of reweighting deficits across a variety of static and dynamic postural tasks.

This study, therefore, aimed to evaluate the influence of repeated exposure to vestibular sensory illusions on control of an anticipatory postural task, comparing individuals with PD to healthy young and age-matched controls. We hypothesized that acute exposure to GVS would deleteriously affect postural control in each group, but that subjects would habituate to the sensory illusion with repeated exposure and that individuals with PD would demonstrate less robust adaptive responses. We further hypothesized that postural responses in individuals with PD would be smaller and slower during the RTT task, compared to age-matched and healthy young controls.

Methods

The current investigation was a repeated measures design to determine whether the repeated application of GVS applied immediately before an anticipatory postural task influenced control of that task.

Participants

Three groups of participants were recruited for this study. These included 1) individuals with idiopathic Parkinson disease (PD group) recruited from a database of current and former patients in our movement disorders clinic, 2) healthy young adults (HY group) between the ages of 18 and 40 recruited from the university campus and surrounding community, and 3) healthy, age-matched (±4 yrs) control participants (HE group) recruited from the local community. Individuals with PD who had not previously had surgical management of their symptoms and who had mild to moderate disease severity (Hoehn and Yahr scale score I-III) were recruited for the study. Additionally, all subjects had to be free of additional neuro-otologic or neurological impairment (ie, neuropathy, stroke, or traumatic brain injury) or recent major lower extremity orthopedic injury or disease (ie, fracture or severe osteoarthritis). Potential subjects who had lower extremity orthopedic surgical procedures within the previous 12 months were also excluded. Finally, all subjects had to be able to understand and follow instructions and not have any physical or cognitive limitation that prevented them from performing the rise to toes task. Exclusion criteria were assessed by having potential subjects complete a self-report questionnaire of medical and surgical history (including questions on any history of inner ear injury or disease that affected balance) and undergo a screening examination that included reflex testing (recorded as absent, diminished, normal, or

exaggerated), Semmes-Weinstein monofilament testing (recorded as present or absent using a 5.56 / 10g monofilament) to assess light touch perception, and quantitative vibration threshold testing using a Rydel Seiffer graduated tuning fork (recorded as normal or abnormal using a cutoff threshold of > 4 to be considered normal).

Instrumentation and Task

All testing was performed over 2 days in the Motion Capture Laboratory in our department using a 10-camera Vicon Motion Analysis System (Vicon Motion Systems, Centennial, CO, USA) and an AMTI OR6-7 series force platform (Advanced Medical Technologies Inc, Watertown, MA, USA). Participants were fitted with a standardized full-body gait analysis set of 55 reflective markers defining 15 body segments (Plug-In Gait marker set; Vicon Motion Systems, Centennial, CO) to quantify kinematics during the task.

A rise to toes (RTT) task was employed to study anticipatory postural control. For the RTT, all participants began in a quiet stance position. A custom written program in Labview (National Instruments Corporation Austin, TX, USA) randomly triggered a light to turn on after at least 6 seconds of quiet standing and turn off after an additional 5 seconds. Participants were instructed to rise onto their toes and hold that position from the time the light turned on until it shut off when they were told to return to quiet standing. This task was chosen because it requires subjects to move between a stable (quiet standing) and unstable (standing on forefoot only) posture. This task has been used previously to study postural control.[18-20]

Bipolar galvanic vestibular stimulation (GVS) was applied over the bilateral mastoid processes using an isolated constant current stimulator (Grass Technologies,

West Warwick, RI). A 1.5 mA, 50 Hz stimulus was applied to each participant with 3 cm^2 electrode pairs with the cathode on the left side for .5 seconds beginning 200 ms prior to initiating the RTT task (Figure 2.1). This paradigm was chosen to determine whether a vestibular-evoked sensory illusion that occurred simultaneously with an anticipatory postural control task would influence the subsequent postural response to that task and, if so, whether the illusion would be suppressed with repeated exposure.

Procedures

All participants read and signed an informed consent document approved by the university IRB prior to participating in the study. Individuals with PD completed the motor component of the Movement Disorders Society Unified Parkinson Disease Rating Scale (MDS-UPDRS). Additionally, individuals in the PD and HE groups completed the functional gait assessment (FGA). Subjects in the HY group were not required to complete the FGA because of potential ceiling effects associated with the instrument for individuals in this age group. During testing, subjects wore form-fitting clothing and no shoes. Participants' height and weight were recorded. Butcher block paper was affixed to the force platform and participants were asked to stand on the platform with the medial border of their feet positioned 10 cm apart in order to quantify center of pressure (COP) during the task. Tracings of their feet were then made on the paper to ensure all trials occurred from the same starting position. In order to control for dopamine replacement medication effects, participants with PD were tested in an off-medication condition at least 12 hours after their last scheduled dosage.[21]

A motor learning paradigm was employed in this study, using an acquisition phase and a retention phase.[22] During the acquisition phase (Day 1), participants

completed three RTT trails with their normal compliment of sensory inputs. Subsequently, participants completed RTT 15 trials with simultaneous GVS separated into five blocks of three trials. To avoid fatigue, participants were provided 30-second rest periods between each block of trials. During the retention phase (48 hours later), participants completed nine RTT trials with GVS, segregated into three blocks and including rest periods as previously described. For each trial, data were collected from trial initiation until the end of the RTT task (return to quiet stance). In order to prevent a fall if the participant was unable to maintain balance during the RTT task, a secondary restraint was worn and a spotter was present to assist balance recovery as needed.

Data Processing and Analysis

Kinematic (COM) and kinetic (COP) data were sampled at 200 Hz and were postprocessed using Vicon Nexus (Vicon Motion Systems, Centennial, CO, USA) and Visual 3D (C-Motion Inc, Germantown, MD, USA) software. Kinetic and kinematic data were lowpass filtered at 15 Hz and 6 Hz, respectively, using a 4^{th} order zero phase lag Butterworth filter. The decision to use these filtering parameters was based on visual inspection of the data and the residual analysis procedure for filter frequencies described by Winter.[23] Independent variables used for analysis were group assignment (HY group, PD group, and HE group) and five time points from the acquisition and retention phases. These were 1) Baseline Block trials (No Stim), 2) Acquisition Block-1 stimulation trials (Early), 3) Acquisition Block-3 stimulation trials (Mid), 4) Acquisition Block-5 stimulation trials (Late), and 5) Retention Block-2 stimulation trials (Retention). The middle block of trials was chosen during retention to avoid transient motor learning factors such as warm-up decrement and fatigue from artificially influencing subject

performance.[24] Five dependent variables of interest were considered to assess the influence of the independent variables on motor planning, postural preparation, postural coordination, and postural stability.

Reaction time measured the time between the trigger (light turning on) and onset of COP movement. This variable served to assess overall motor planning.[19] Longer times to movement onset were associated with increased motor planning demands.

Postural preparation was assessed by measuring the anticipatory postural adjustment (APA) associated with the movement from quiet stance to toe rise. The APA was calculated as the greatest posterior COP displacement in the sagittal plane between the trigger and the beginning of anterior COP displacement. A larger APA was interpreted as better postural preparation, while a smaller APA was interpreted as hypokinetic preparation.[25]

Postural coordination was assessed during the movement from foot flat to toe rise using two variables, COP velocity and the COP / COM difference. Center of pressure velocity was calculated as the rate of change of the net COP during the initial 0.25 seconds of anterior COP displacement.[19] Greater COP velocity was interpreted as improved postural coordination, while decreased velocity was interpreted as bradykinetic postural coordination.[19] The COP-COM difference was calculated as the greatest difference between COP and the vertical projection of the COM onto the floor in the sagittal plane between rise trigger and peak heel height during the initial 0.25 seconds of anterior COP displacement. A larger separation between COP and COM was interpreted as better postural coordination as supported by previous research.[19,20]

Postural stability was assessed by calculating the coefficient of variation (CV)

associated with the vertical heel position. The CV was calculated by dividing the standard deviation of heel position by average heel position during the middle 3 seconds of the RTT task. A larger coefficient of variation was interpreted as reduced postural stability.

Each variable was compared across five time points as outlined previously using blocked averages from three consecutive trials. The block of non-GVS trials (No-Stim) was compared to Early, Mid, and Late blocks of GVS trials during the acquisition phase to identify changes in performance that may have occurred with exposure to repeated sensory illusions. The No-Stim block was also compared to the retention block to determine if motor learning had taken place.

Data were analyzed using separate, 3x5 mixed model analyses of variance (ANOVA) with repeated measures on the time factor. In the event of a significant finding in the omnibus F tests, post-hoc tests were performed using Bonferroni correction to correct for multiple comparisons of main effects between and within subjects. The initial level of significance for all comparisons was set at 0.05. All statistical analyses were performed with SPSS 19 (IBM Inc; Armonk, NY,USA). Effect sizes were calculated to assess standardized mean differences between groups and across time. To control for inflation of the effect size due to a small sample size Hedge's g was calculated for between group differences (annotated hereafter as g_s) and within group differences across time (annotated hereafter as g_{av}) in accordance with the guidelines reviewed by Lakens et al.[26] Hedge's g is a corollary of Cohen's d, used for small sample sizes, and as such ranges from 0 to infinity and is interpreted as a percentage of the standard deviation (ie, $g_s = 0.5$ means the effect size is half the standard deviation). In order to simplify interpretation of the effect sizes, we also calculated the common language effect size

(CL). The CL is expressed as a percentage and expresses the likelihood that an individual from one group (or measurement from one time point) will differ from an individual from another group (or measurement from another time point).[26] A CL effect size of 50% indicates that the likelihood of one observation being different from another is no better than chance (ie, flipping a coin and having it come up heads). We used the convention that a CL effect size ≥ 70% would relate to a clinically meaningful difference between observations (ie, 20% above a chance difference).

Results

Twenty-seven individuals with PD, 22 healthy elderly adults, and 17 healthy young adults were screened for inclusion in this study. Among individuals with PD who were excluded from the study, three had had surgery for their PD symptoms, four had a comorbid peripheral neuropathy, and eight had a Hoehn & Yahr score greater than III. Eleven elderly adults were excluded from participation due to recent orthopedic surgery (n = 3), peripheral neuropathy (n = 5), and severe arthritis (n = 3). Two young adults were excluded from the study due to recent orthopedic injuries that affected their balance. Thirty-five participants completed testing. Data for one individual in the HE group were corrupted and unable to be used for analysis. Therefore, analyses were performed on 34 participants. Participant characteristics are presented in Table 3.1.

Motor Planning

There was a significant group by time interaction for reaction time ($F = 4.05$. $df = 2.4$, $p = .003$, Figure 3.1). Post-hoc comparisons demonstrated that in the HY group, compared to reaction time in the nonstimulated block ($\overline{x}$ = .56 sec, CI_{95} = .49-.62 sec),

Table 3.1: Participant Characteristics (N=36)

	HY (N=15) $\overline{x}$ (95% CI)	PD (N=11) $\overline{x}$ (95% CI)	HE (N=10) $\overline{x}$ (95% CI)
Age (yrs)	25.6 (24.4-26.8)	69 (64.2-73.8)	63.9 (57.9-70.3)
Hgt(cm)	172.9 (166.3-179.4)	172.3 (166.4-178.1)	174.5 (170.6-178.3)
Wgt(kg)	74.7 (62.9-86.4)	80.1 (73.3-86.9)	91.4 (77.9-104.8)
FGA	--- NA ---	24.7 (23.2-26.2)	27.9 (26.3-29.5)
UPDRS	--- NA ---	17.7 (11.5-23.9)	--- NA ---

FGA – Functional Gait Assessment

UPDRS – Motor Subcomponent of Movement Disorders Society Unified Parkinson Disease Rating Scale

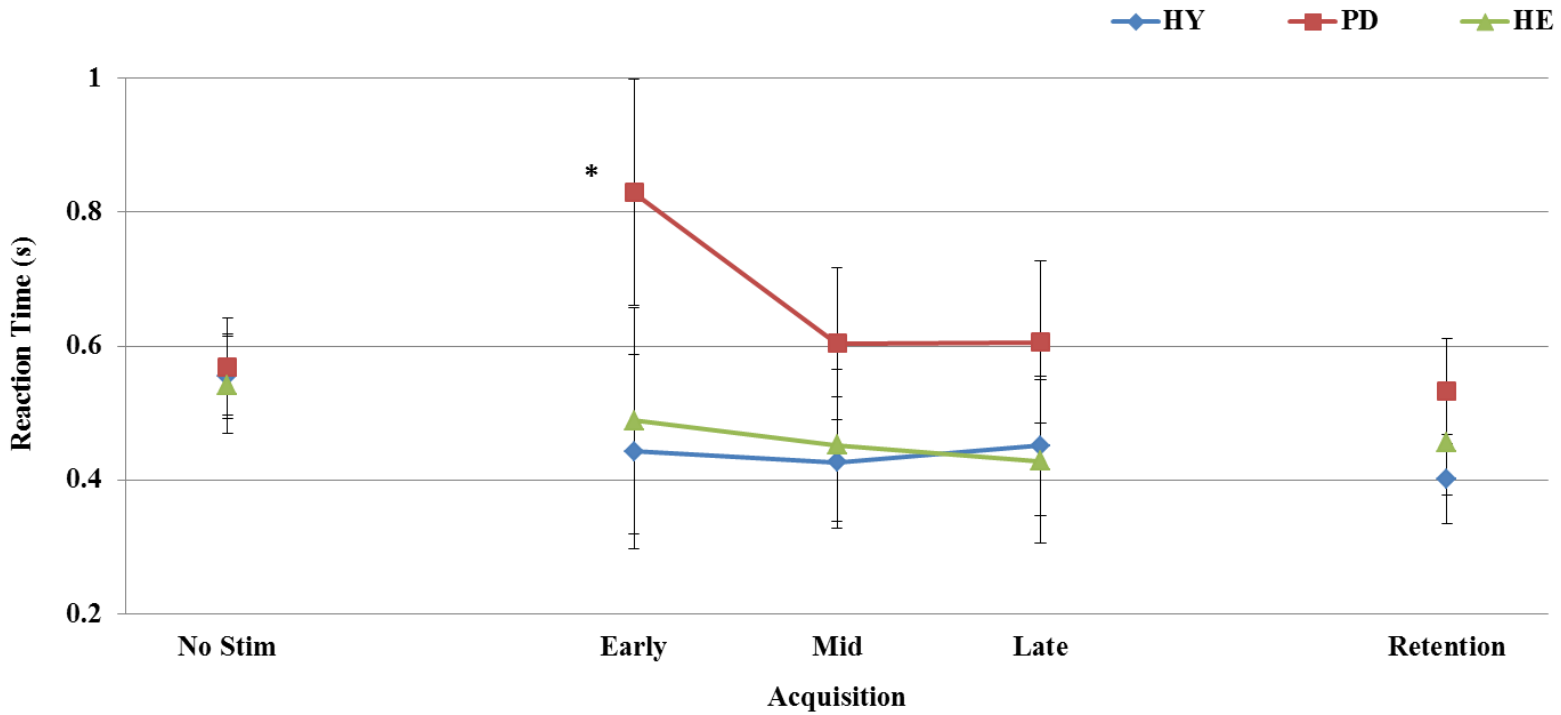

Figure 3.1: Average Group Reaction Times (s) at Prestimulation, Acquisition, and Retention
* Significant increase in reaction time at Early Acquisition in PD Group

reaction time at retention was significantly faster (Mean difference and 95% Confidence interval; $\overline{x}_{diff}$ = .15 sec, CI_{95} = .04-.27 sec, p = .004). In contrast, in the PD group, reaction times during early acquisition ($\overline{x}$ = .83 sec, CI_{95} = .65-.1.0 sec) were significantly longer compared to No-Stim ($\overline{x}_{diff}$ = .26 sec, CI_{95} = .02-.50 sec, p= .028), MID ($\overline{x}_{diff}$ = .23 sec, CI_{95} = .06-.39 sec, p = .003), LATE ($\overline{x}_{diff}$ = .22 sec, CI_{95} = .06-.38 sec, p = .002), or RET ($\overline{x}_{diff}$ = .30 sec, CI_{95} = .09-.50 sec, p = .001) blocks. Reaction time in the HE group did not differ across time. Within group effect sizes (Hedge's g_{av}) in the HY group, comparing reaction time in the nonstimulated trial block to acquisition and retention blocks were large, ranging from 1.14-2.42. The corresponding CL effect sizes indicated that the likelihood that a reaction time for someone in this group would be faster during acquisition or retention blocks compared to the nonstimulated block ranged from 84%-96%. Effect sizes for the PD and HE groups were generally lower (Table 3.2).

There was also a significant group effect for reaction time (F = 4.1, df = 2, p = .025; Table 3.3). Post-hoc comparisons showed that the reaction time in the PD group was significantly longer than that in the HY group (Mean difference and 95% Confidence interval; $\overline{x}_{diff}$ = .17 sec, CI_{95} = .01-.33 sec, p = .031). Effect sizes comparing the PD group to the HY and HE groups were large (g_s = .1.03 and .93, respectively). The between group CL effect sizes showed that the likelihood that someone from the PD group would have a longer reaction time than someone from the HY group was 77%. This likelihood was 75% when comparing individuals in the PD and HE groups, despite a lack of statistical significance between these two groups (Table 3.3).

Table 3.2: Effect Size Indices Comparing Baseline (No Stim) Block to Acquisition and Retention Blocks

	Acquisition						Retention	
	Early		Mid		Late			
HY	g_s	CL	g_s	CL	g_s	CL	g_s	CL
Reaction Time	1.31	86%	1.41	87%	1.14	84%	2.42	96%
APA	.12	57%	.27	64%	.24	60%	.19	57%
COP Velocity	.20	71%	.27	63%	.01	50%	.09	53%
COP-COM Difference	.36	68%	.11	53%	.10	53%	.31	65%
Heel Raise CV	.32	67%	.23	63%	.31	61%	.56	65%
PD								
Reaction Time	.81	73%	.17	56%	.16	55%	.23	62%
APA	.53	70%	.12	55%	.09	54%	.42	64%
COP Velocity	.11	59%	.14	58%	0.0	50%	.24	60%
COP-COM Difference	.18	61%	.21	59%	.14	56%	.60	67%
Heel Raise CV	1.12	79%	.10	53%	.13	54%	.02	51%
HE								
Reaction Time	.33	60%	.49	75%	.74	77%	.54	66%
APA	.13	56%	.14	56%	.14	58%	.01	50%
COP Velocity	.01	52%	.12	58%	.02	51%	.12	59%
COP-COM Difference	.06	55%	.17	63%	.22	68%	.05	53%
Heel Raise CV	.06	52%	.52	67%	.50	69%	.15	56%

g_{av} Hedges g effect size index CL Common Language effect size index

Table 3.3: Between Group Comparisons (Mean [95% CI]) and Effect Size Indices

	HY	PD	HE	HY:PD		HE:PD		HY:HE	
	$\overline{x}$ (95% CI)	$\overline{x}$ (95% CI)	$\overline{x}$ (95% CI)	g_s	CL	g_s	CL	g_s	CL
Reaction Time (s)*	**.46 (.37-54)**	.63 (.53-.73)	.47 (.38-.57)	1.03	77%	.93	75%	.11	53%
APA*	**.039 (.033-.045)**	.025 (.018-.031)	**.039 (.032-.046)**	1.18	80%	1.19	81%	.01	50%
COP Velocity*	**.81 (.69-.93)**	.34 (.21-.47)	**.61 (.47-.74)**	2.11	94%	1.19	81%	.91	75%
COP-COM Difference*	**6.19 (5.51-6.87)**	3.89 (3.14-4.66)	5.09 (4.30-5.88)	1.72	90%	.92	75%	.84	73%
Heel Raise CV*	**.03 (.01-.06)**	.10 (.07-.12)	.08 (.06-.11)	1.39	84%	.30	58%	1.37	85%

* significant group main effect, post-hoc difference from PD group is in in **BOLD,** post-hoc difference from HE group is Underlined

$\overline{x}$ Mean

CI Confidence interval

g_s Hedges g between group effect size index

CL Common Language effect size index

Postural Preparation

There were no interaction effects for anticipatory postural adjustment (Figure 3.2). There was a significant group effect for the anticipatory postural adjustment ($F = 6.2$, $df = 2$, $p = .005$; Table 3.3). Post-hoc comparisons demonstrated that the PD group ($\overline{x} = .025$ m, $CI_{95} = .02$-$.03$ m) had a significantly smaller APA than either the HY group ($\overline{x}_{diff} = .014$ m, $CI_{95} = .003$-$.026$ m, $p = .009$) or HE group ($\overline{x}_{diff} = .014$ m, $CI_{95} = .002$-$.026$ m, $p = .017$). Effect sizes comparing the PD group to the HY and HE groups were large ($g_s = 1.18$ and 1.19, respectively). The between group CL effect sizes showed that the likelihoods that someone from the PD group would have a smaller APA than someone from the HY or HE groups were 80% and 81%, respectively (Table 3.2).

There was also a significant main effect of time ($F = 2.8$, $df = 3.3$, $p = .038$), but post-hoc comparisons failed to show significant differences between individual time points. Effect sizes comparing the nonstimulated block with acquisition and retention blocks were generally small (Table 3.2).

Postural Coordination

There were no interaction or main effects for time for COP velocity (Figure 3.3). Within subject effect sizes tended to be small across acquisition and retention blocks in each group. There was a significant group effect for COP velocity ($F = 14.9$, $df = 2$, $p < .001$). Post-hoc comparisons demonstrated that the PD group ($\overline{x} = .34$ m/s, $CI_{95} = .21$-$.47$ m/s) had significantly slower peak velocity than either the HY group ($\overline{x}_{diff} = .47$ m/s, $CI_{95} = .25$-$.69$ m/s, $p < .001$) or the HE group ($\overline{x}_{diff} = .27$ m/s, $CI_{95} = .04$-$.50$ m/s). Effect sizes comparing the PD group to the HY and HE groups were large ($g_s = 2.11$ and 1.19, respectively). The between group CL effect sizes showed that the likelihoods that

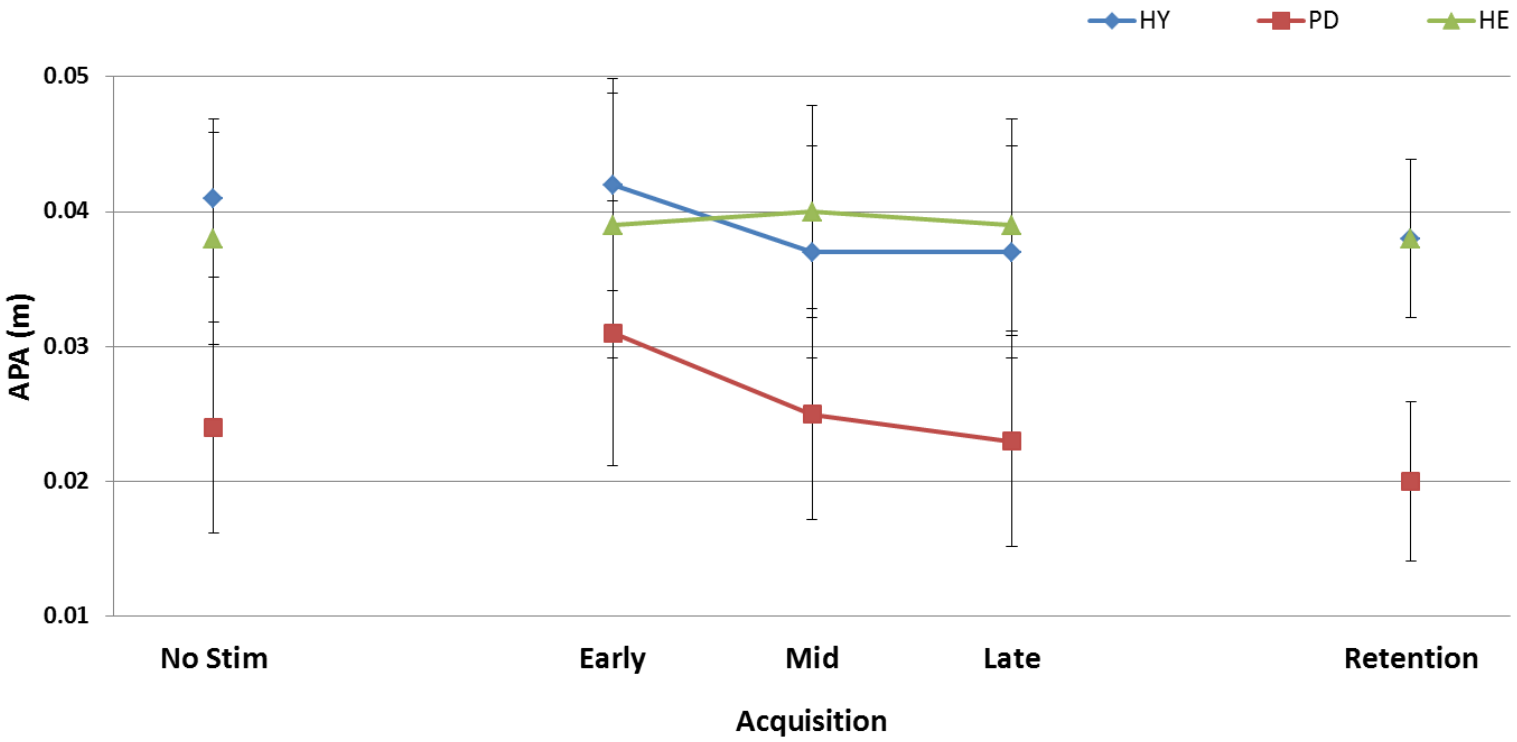

Figure 3.2: Average Group APA (m) at Prestimulation, Acquisition, and Retention

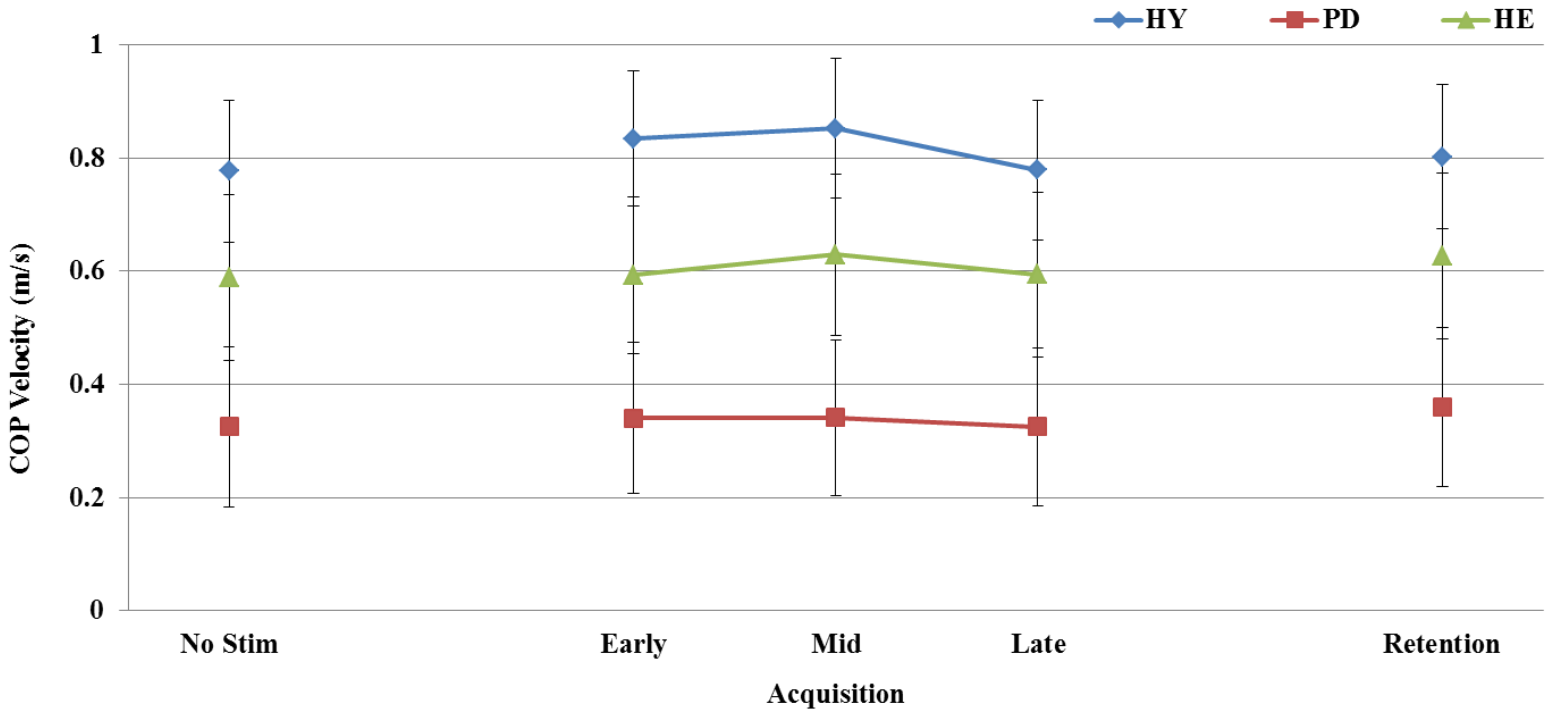

Figure 3.3: Average Group COP Velocity (m/s) at Prestimulation, Acquisition, and Retention

someone from the PD group would have a lower COP velocity than someone from the HY or HE groups were 94% and 81%, respectively (Table 3.3). Despite a lack of statistical significance between the HY and HE groups, effect sizes were still large (g_s =.91; CL = 75%), demonstrating that a clinically meaningful difference exists between age groups.

There were no interaction or main effects for time for COP-COM difference (Figure 3.4). There was a significant group effect for COP-COM difference (F = 10.5, df = 2, p < .001). Post-hoc comparisons demonstrated that the PD group ($\overline{x}$ = 3.89 cm, CI_{95} = 3.14-4.66 cm) had significantly smaller COP-COM separation than the HY group ($\overline{x}_{diff}$ = 2.29 cm, CI_{95} = 1.03-3.55 cm, p < .001) but not the HE group ($\overline{x}_{diff}$ = 1.19 cm, CI_{95} = -.16-2.55 cm). The effect sizes (Table 3.3) comparing the PD group to the HY group were large (g_s =1.72; CL = 90%)). Despite a lack of statistical significance between the HE and PD or HY groups, effect sizes were still large (g_s =.92 and .84, respectively). Additionally, CL effect sizes demonstrated that the likelihood of someone in the HE group having a larger COP-COM separation than someone in the PD group was 75%, and having a smaller difference than someone in the HY group was 73%. These values suggest that there is a clinically meaningful effect of age and disease on COP-COM separation.

Postural Stability

There was a significant group by time interaction for heel height CV (F = 5.34, df = 2.9, p = .002, Figure 3.5). Post-hoc comparisons demonstrated that in the PD group, heel height CV during early acquisition ($\overline{x}$ = .17, CI_{95} = .12-.21) was significantly greater compared to No-Stim ($\overline{x}_{diff}$ = .09, CI_{95} = .02-.15, p = .003), MID ($\overline{x}_{diff}$ = .08, CI_{95} = .02-

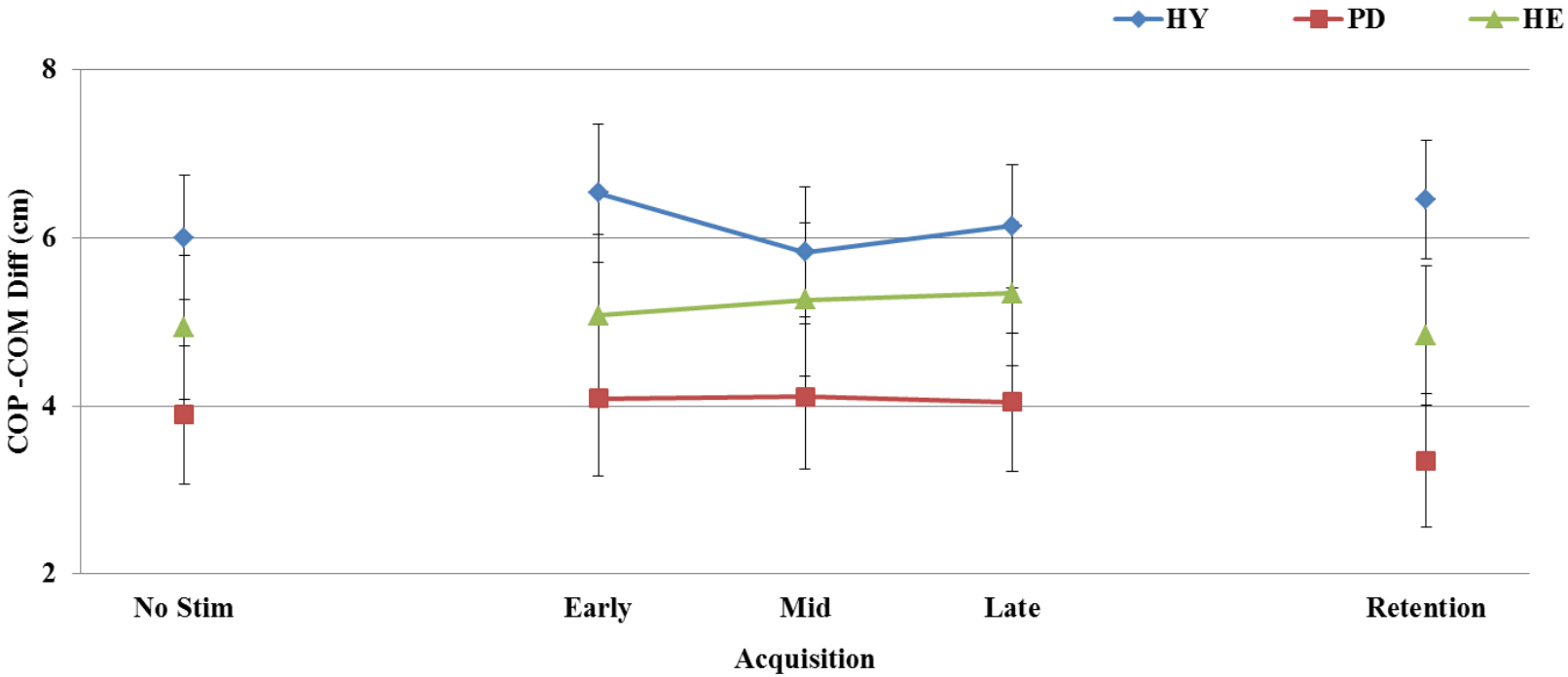

Figure 3.4: Average Group COP-COM Difference (cm) at Prestimulation, Acquisition, and Retention

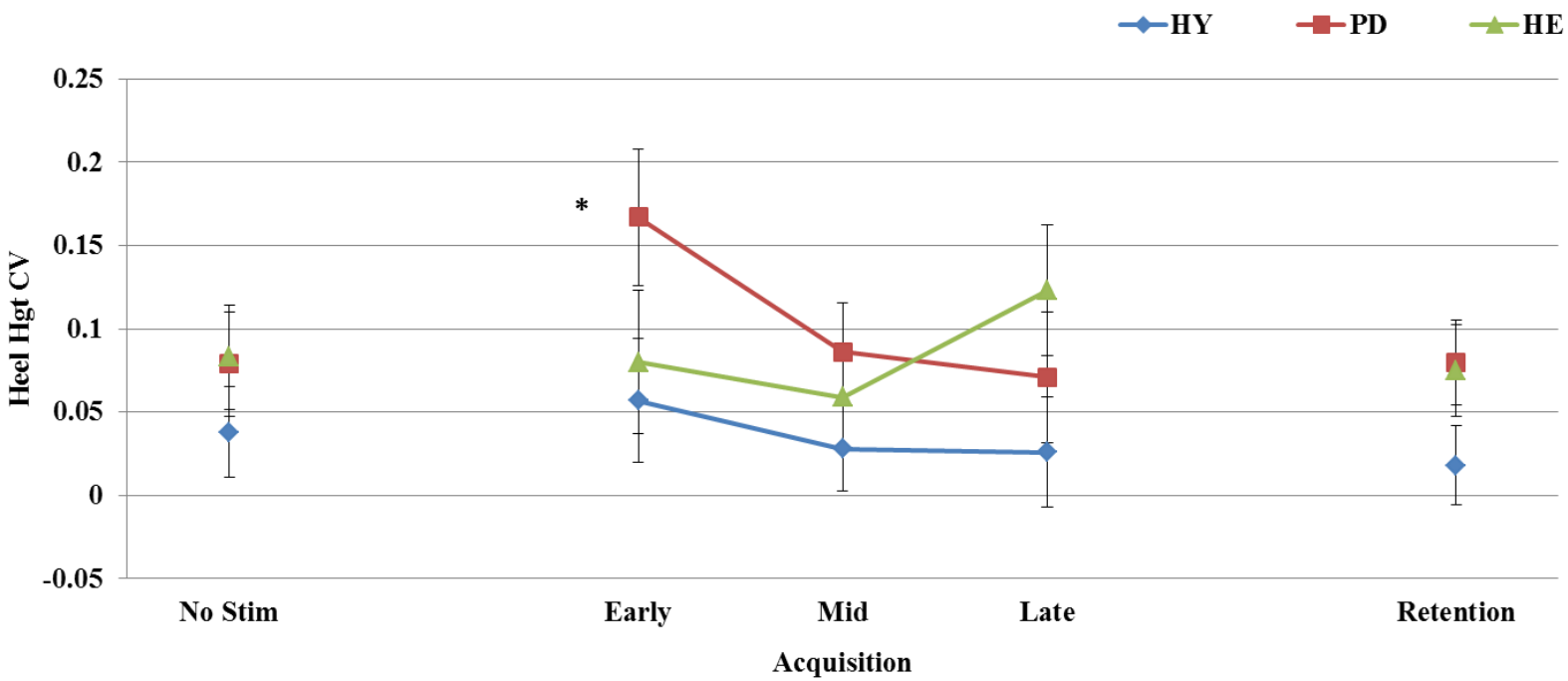

Figure 3.5: Average Group Heel Height CV at Prestimulation, Acquisition, and Retention
* Significant increase in reaction time at Early Acquisition in PD Group

.15, p = .004), LATE ($\overline{x}_{diff}$ = .10, CI_{95} = .02-.17, p = .004), or RET ($\overline{x}_{diff}$ = .09, CI_{95} = .02-.16, p = .005) blocks. Heel height CV did not differ across time in the HY or HE groups. Within group effect sizes comparing heel height CV in the nonstimulated trial block to acquisition and retention blocks were generally small across groups, with the exception of the PD comparison of nonstimulated to early acquisition blocks (Table 3.2).

There was also a significant group effect for heel height CV (F = 9.09, df = 2, p = .001; Table 3.3). Post-hoc comparisons showed that the heel height CV in the HY group ($\overline{x}$ = .033, CI_{95} = .012-.055) was significantly smaller than that in the PD group ($\overline{x}_{diff}$ = .06, CI_{95} = .02-.23, p = .001) and the HE group ($\overline{x}_{diff}$ = .05, CI_{95} = .01-.09, p = .01). Effect sizes comparing the HY group to the PD and HE groups were large (g_s = .1.39 and 1.37, respectively). The between group CL effect sizes showed that the likelihood that someone from the HY group would have a smaller heel height CV than someone from the PD group was 84%, and this value was 85% when comparing someone from the HE group (Table 3.3).

Discussion

This study sought to assess the influence of repeated exposure to GVS on postural responses associated with an anticipatory postural task in individuals with PD, healthy young adults, and healthy older adults. We hypothesized that initial exposure to a sensory illusion would result in a deterioration of performance across groups, but that repeated exposure to the illusion would produce postural adaptations that would result in improved performance. We further hypothesized that postural responses in individuals with PD would be hypokinetic and bradykinetic compared to controls. We employed a classic motor learning paradigm in which subjects underwent a large series of practice trials on

one day followed by a smaller series of trials on a subsequent day. We found that acute exposure to GVS differentially affected motor planning, postural preparation, and postural stability in individuals with PD compared to controls. We further observed that repeated exposure to GVS reulted in adaptive changes in these components of postural control in individuals with PD. We also report that individuals with PD demonstrated a paucity of movement, slowness of movement, and impaired stability with a rise to toes task.

Acute Influence of GVS on Postural Recovery

Acute exposure to GVS resulted in impaired motor planning (Figure 3.1), a small but potentially meaningful abberation in postural preparation (Figure 3.2; Table 3.2), and decreased postural stability (Figure 3.5) in the PD group, while similar findings were not observed in controls. In fact, we found that reaction time actually decreased in the HY group during acute GVS exposure (Figure 3.1; Table 3.2). Evaluation of individual trials in the HY group showed that this finding reflected a tendency to adapt to GVS within the first 1-2 trials and, we believe, subsequently incorporate the GVS into their motor program as a trigger to rise to toes. These findings appear to indicate that while healthy controls are able to effectively suppress or even leverage exposure to an acute sensory illusion, individuals with PD are unable to suppress abberant sensory input during a dynamic postural activity. Our results extend findings reported elsewhere, which have shown similar deficits in individuals with PD when faced with acute postural perturbations.[25,27,28]

Influence of Repeated Exposure to GVS on Postural Adaptation

With repeated exposure to GVS, individuals with PD seemed to implicitly learn to suppress the sensory illusion as evidenced by improved motor planning (Figure 3.1), restoration of normal postural preparation (Figure 3.2), and improved postural stability (Figure 3.5) at later acquisition and retention time points compared to early acquistion. Healthy controls did not demonstrate changes in postural control across acquisition and retention with one notable exception. Both of the control groups demonstrated a tendency to incorporate the GVS into their motor program as a trigger to rise to toes as evidenced by a decrease in reaction times. Individuals in the HY group, who first showed this tendency with acute exposure improved in this ability throughout acquisition and carried it over to retention, while those in the HE group had more modest incorporation at later acquisition time points that did not saliently persist at retention.

The differences observed in the patterns of postrual control responses across groups during acquisition and retention demonstrate that when confronted with repeated sensory illusion exposure, individuals with PD were able implicitly to learn to suppress abberant sensory cues in a similar manner, albeit not as quickly, or to the same extent as controls. This suggests that the ability to reweight sensory stimuli to improve postural control is impaired in individuals with PD, but still present.[29] These findings are of particular interest because they indicate that sensory illusion training results in adaptation of postural responses in PD, which may provide new avenues to augment balance training programs in rehabilitation.

Based on the few changes in postural responses either acutely or following repeated exposure to GVS exhibited by healthy controls, our findings may also suggest

that the healthy nervous system rapidly suppresses vestibular illusions when performing a voluntary postural task that requires a planned change or reduction in the BOS. In this context the CNS may rely more heavily on somatosensory or visual information to meet the objectives of the task.[30]

Influence of PD and Age on Postural Responses During RTT

In the current study, we observed that during a rise to toes task, postural preparation and at least one facet of postural coordination (COP velocity) were significantly impaired in persons with PD in comparison to young and elderly controls. In addition, persons with PD were significantly impaired in motor planning, postural coordination (as measured by COP-COM difference), and postural stability compared to young healthy controls and the former two variables demonstrated clinically meaningful deficits compared to healthy elders (Table 3.3). Our findings extend previous research, which has shown that individuals with PD demonstrate prolonged motor programming time,[19,31] hypokinetic movement preparation,[19,20,31] and diminished postural coordination and stability[19,20,32] compared to controls.

Our findings also showed that postural coordination and stability decline with age in a clinically meaningful way (Table 3.3). Previous research has shown that postural coordination (as measured by COP velocity and COP-COM separation) is reduced in older healthy adults,[18] which supports our findings of clinically meaningful, albeit statistically nonsignificant, deficits associated with age in these variables. In contrast to previous research in our lab that failed to find age-related differences in postural stability during a rise to toes task,[19] we identified significant increases in these variables in older adults.

Taken together, our results indicate that some postural control deficits in PD during a RTT task are compounded by age-related declines. Specifically, slower movement, reduced separation of the COP and COM, and the reduced ability to maintain steady heel height may represent declines in physical factors, such as strength or agility, as well as deficits in the production of postural synergies during movement among older individuals which are compounded in PD. The combination of these deficits, in turn, progressively diminishes the ability of these groups to execute the RTT task.[33,34]

Limitations and Future Research

This study assessed the differential postural responses of individuals with PD and healthy controls to acute and repeated exposure to a vestibular sensory illusion. Age matching was imperfect in the current study, which potentially limited our ability to discern between age-related and PD-related differences in postural control following acute or repeated GVS application. In order to mitigate this weakness in our study we conducted separate ANCOVAs for each variable of interest, comparing individuals with PD and healthy elders using age as a covariate. Results of these analyses did not differ from results of similarly conducted ANOVAs comparing these groups. Therefore, we believe age did not confound our results and our interpretation of differences attributed to age or PD are correct. Future research should seek to confirm our findings in a larger cohort of individuals with PD and healthy elders using a tighter restriction on age-matching.

Another potential limitation of the current research was the failure to include a group of individuals with advanced PD who would be more likely to demonstrate greater postural instability. We chose instead to study individuals with mild to moderate disease

because we felt that these individuals would most likely demonstrate adaptive change. We could also be criticized for utilizing a stimulus that either due to intensity or duration did not negatively influence postural control in healthy young subjects. However, our goal was to determine if a sensory illusion presented immediately before and during initiation of an anticipatory postural task would influence the execution of that task. Using a longer duration stimulus would have allowed subjects more time to compensate for the illusion before initiating the RTT task if the stimulus began earlier or interfered with later components of the RTT task (ie, active compensation of GVS while in the "on toes" position). Due to the short duration of the stimulus, increasing the amplitude would have potentially evoked pain and confounded our results. Therefore, we deemed the reported methods as the most appropriate way to meet our study objective.

Future research should investigate postural responses to GVS during anticipatory tasks in individuals with a broader spectrum of postural control issues (ie, orthopedic, neurologic, and age-related). Additionally, given that our findings were consistent with the hypothesis that markers of postural coordination and stability are more sensitive to age-related declines than are markers of motor planning and movement preparation, future research should consider these constructs as a means to assess postural decline longitudinally.

Conclusion

Individuals with PD show marked deficits in postural control of an anticipatory balance task compared to healthy young and age-matched controls, while fewer age-related differences were found among healthy adults. Repeated exposure to short duration galvanic vestibular stimulation resulted in rapid adaptations in healthy controls, but

slower adaptive changes in individuals with PD. Reweighting of sensory signals associated with an anticipatory postural task appears intact in individuals with PD, but adaptive responses require a greater amount of exposure to the sensory illusion.

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CHAPTER 4

EFFECTS OF A VESTIBULAR SENSORY ILLUSION COUPLED WITH A REACTIVE POSTURAL TASK ON ACUTE AND ADAPTIVE RESPONSES IN PARKINSON DISEASE AND HEALTHY ADULTS

Abstract

Postural stability is compromised in persons with Parkinson disease (PD), in part to impairments in sensory organization. However, little is known about the ability of these individuals to adapt to erroneous sensory cues, particularly during tasks which involve reaction to an unexpected perturbation. The purpose of this study was to determine whether repeated exposure to a vestibular sensory illusion coupled with a reactive postural control task would differentially influence acute or adaptive postural responses in healthy young adults, healthy older adults, and individuals with Parkinson disease. Measures of postural coordination decreased in individuals with PD with acute exposure to GVS, while postural control and base of support (BOS) transition were unaffected initially. Repeated exposure to GVS in these individuals demonstrated persistent adaptive changes in postural coordination and an adaptive trend in BOS transition. Acute and repeated GVS exposure did not influence postural responses in healthy controls. Taken together, it appeared that persons with PD developed a

protective strategy to accommodate a smaller step length in light of the impending threat to posterior balance loss that coincided with or rapidly followed GVS. We believe, given that posterior postural stability is diminished in PD, these individuals likely experienced a greater postural threat to the tether release than did controls. The increased threat, in turn, may have provoked the compensation we observed in these subjects.

Introduction

Parkinson disease is one of the most common movement disorders, with a worldwide prevalence of approximately .1-.3% per 100,000.[1] The clinical presentation of PD includes hallmark motor signs of tremor, rigidity, akinesia, bradykinesia, and postural instability. Among these motor signs, postural instability has the most serious implications for morbidity and mortality due to its resistance to pharmacologic therapy and the direct relationship between deterioration of postural stability and injurious falls leading to fracture, reduced mobility, and functional decline.[2-4]

Postural instability in PD is compounded by impairment of sensory integration associated with loss of dopaminergic pathways.[5] Postural stability is predicated upon the central nervous system's ability to produce appropriate motor responses to a changing external environment. In order to accomplish this, the CNS relies on the integration of sensory information about the relationship between the internal state of the body and the changing external environment. Sensory integration is adaptive, such that when one sensory system is unable to provide accurate information, it is downregulated and other sensory modalities are simultaneously upregulated to ensure postural equilibrium is maintained, a phenomenon known as sensory reweighting.[6-8] In PD, proprioceptive input is thought to be compromised and by extension, the ability to reweight sensory

information may be impaired.[5]

Sensory reweighting is studied by manipulating one or more sensory systems to reduce the amount or accuracy of the information it provides (ie, altering visual and proprioceptive input by having a person close their eyes and stand on a foam surface).[7] This manipulation is called a sensory illusion. When one sensory modality is impaired, the manipulation of remaining, intact modalities may provide information on the extent of the deficit or the adaptability of the overall system.[9] Galvanic vestibular stimulation (GVS) provides a means of selectively producing vestibular illusions by using a low amplitude electrical impulse to evoke the sensation of a change in head on body orientation.[10,11] As evidence of the adaptability of the nervous system to sensory changes, sensitivity to GVS is increased in individuals with diminished peripheral somatosensation.[12] Additionally, short-term adaptive changes[13] as well as motor learning effects[14] in response to GVS have been demonstrated in healthy adults following repeated exposure. It is currently unknown whether sensitivity to GVS is altered in PD where sensory integration is impaired or whether adaptive changes may occur with repeated exposure, given the deficits in motor learning associated with the disease.[15]

In order to study the adaptability of PD to vestibular sensory illusions evoked by GVS, it is important to assess responses not only during static stance, but also during anticipatory and reactive tasks. While postural instability in PD is multidirectional,[16,17] it appears to be most pronounced posteriorly.[18,19] Therefore, in the current study, we sought to determine whether repeated exposure to vestibular sensory illusions immediately prior to a reactive postural control task would influence postural responses differently in PD subjects compared to healthy young and age-matched controls. We

employed a tether release task to evoke reactive postural responses. The tether release has been used to evaluate postural responses to a simulated slip or trip in young and older populations.[20,21] We hypothesized that GVS would initially increase postural instability associated with tether release in all subjects, but due to their sensory integration deficits, subjects with PD would adapt with repeated exposure to the sensory illusion more slowly than neurologically healthy controls. We further hypothesized that individuals with PD would demonstrate hypokinesia and bradykinesia compared to age-matched and healthy young controls.

Methods

Design and Participants

The current investigation was a repeated measures design to determine whether the repeated application of GVS applied immediately before a reactive postural control task influenced responses to that task. Three groups of participants were recruited for this study. These included 1) individuals with idiopathic Parkinson disease (PD group) recruited from a database of current and former patients in our movement disorders clinic, 2) healthy young adults (HY group) between the ages of 18 and 40 recruited from the university campus and surrounding community, and 3) healthy, age-matched control participants (HE group) recruited from the local community. Individuals with PD who had not previously had surgical management of their symptoms and who had mild to moderate disease severity (Hoehn and Yahr scale score I-III) were included in the study. Additionally, all subjects had to be free of additional neurological impairment (ie, neuropathy, stroke, neuro-otologic conditions, or traumatic brain injury) and recent major lower extremity orthopedic injury or disease (ie, fracture or severe osteoarthritis).

Potential subjects who had lower extremity orthopedic surgical procedures within the previous 12 months were also excluded. Finally, all subjects had to be able to understand and follow instructions and not have any physical or cognitive limitation that prevented them from performing the tether release task. Exclusion criteria were assessed by having potential subjects complete a self-report questionnaire of medical and surgical history (including questions on any history of inner ear injury or disease that affected balance) and undergo a screening examination that included reflex testing (recorded as absent, diminished, normal, or exaggerated), Semmes-Weinstein monofilament testing (recorded as present or absent using a 5.56 / 10 g monofilament) to assess light touch perception, and quantitative vibration threshold testing using a Rydel Seiffer graduated tuning fork (recorded as normal or abnormal using a cutoff threshold of > 4 to be considered normal).

Instrumentation and Task

All testing was performed over 2 days in the Motion Capture Laboratory in our department using a 10-camera Vicon Motion Analysis System (Vicon Motion Systems, Centennial, CO, USA) and an AMTI OR6-7 series force platform (Advanced Medical Technologies Inc, Watertown, MA, USA). Participants were fitted with a standardized full-body gait analysis set of 55 reflective markers defining 15 body segments (Plug-In Gait marker set; Vicon Motion Systems, Centennial, CO) to quantify kinematics during the task.

A posterior tether release (PTR) task was employed to study reactive postural control.[22] For the PTR, a tether was connected between a chest harness and an electromagnet mounted to the wall. A load cell (iLoad mini, Loadstar Sensors, Fremont, CA, USA) aligned in series with the tether registered the percent body weight placed

against the tether as the subject leaned back against the harness. A custom written program in Labview (National Instruments Corporation Austin, TX, USA) linked the load cell information with the motion capture system. When the subject exerted between 8% and 12% of their body weight against the tether, a computer-generated tone sounded. Upon sounding of a steady tone for at least 6 seconds, the tether was randomly released between the sixth and ninth second of the trial by remote triggering through the Labview program. Release caused a posterior loss of balance, which compelled the subject to take a compensatory step to recover.

In order to produce a vestibular sensory illusion, bipolar galvanic vestibular stimulation (GVS) was applied over the bilateral mastoid processes using an isolated constant current stimulator (Grass Technologies, West Warwick, RI). A 1.5 mA, 50 Hz stimulus was applied to each participant for 500 ms beginning 200 ms prior to tether release using 3 cm^2 electrode pairs with the cathode on the left side (Figure 2.1). A custom written Labview program (National Instruments Corporation Austin, TX, USA) randomly triggered vestibular stimulation within a 2-second window after at least 6 seconds of quiet stance data were collected. This paradigm was chosen to determine whether a vestibular-evoked sensory illusion that occurred immediately prior to and during the initiation of a reactive postural control task would influence the subsequent postural response to that task and, if so, whether the illusion would be suppressed with repeated exposure.

Procedures

All participants read and signed an informed consent document approved by the university IRB prior to participating in the study. Individuals with PD were assessed with

the motor component of the Movement Disorders Society Unified Parkinson Disease Rating Scale (MDS-UPDRS). Additionally, in order to assess fall risk, individuals in the PD and HE groups completed the Functional Gait Assessment (FGA).[23] Subjects in the HY group were not required to complete the FGA because of potential ceiling effects associated with the instrument for individuals in this age group. During testing, subjects wore form-fitting clothing and no shoes. Participant's height and weight were recorded. Butcher block paper was affixed to one force platform and participants were asked to stand on the platform with the medial border of their feet positioned 10 cm apart. Tracings of their feet were then made on the paper to ensure all trials occurred from the same starting position. In order to control for dopamine replacement medication effects, participants with PD were tested in an off-medication condition at least 12 hours after their last scheduled dosage.[23]

A motor learning paradigm was employed in this study, using an acquisition phase and a retention phase.[24] During the acquisition phase (Day 1), participants completed three trials of the PTR with their normal compliment of sensory inputs. Subsequently, participants completed 15 trials of the PTR with GVS separated into five blocks of three trials. To avoid fatigue, participants were provided 30-second rest periods between each block of trials. During the retention phase (48 hours later), participants completed nine trials of PTR with GVS, segregated into three blocks and including rest periods as previously described. For each trial, data were collected from trial initiation (time at which data recording was started and subject given the command to stand still) until the participant arrested posterior movement after the tether release and began to move forward again. In order to prevent a fall in case the participant was unable to

compensate for the posterior loss of balance, a secondary restraint was worn and a spotter was present to assist balance recovery as needed.

All participants stood quietly with their heels no more than 10 cm apart and toes angled outward approximately 20 degrees. Participants were asked to stand with their head facing forward, their eyes open, and arms at their sides. Each trial lasted approximately 25 seconds during which a vestibular sensory illusion was evoked approximately 6 seconds into the trial.

Data Processing and Analysis

Kinematic (COM) and kinetic (COP) data were sampled at 200 Hz and were postprocessed using Vicon Nexus (Vicon Motion Systems, Centennial, CO, USA) and Visual 3D (C-Motion Inc, Germantown, MD, USA) software. Kinetic and kinematic data were lowpass filtered at 15 Hz and 6 Hz, respectively, using a fourth order zero phase lag Butterworth filter. The decision to use these filtering parameters was based on visual inspection of the data and the residual analysis procedure for filter frequencies described by Winter.[25] Independent variables used for analysis were group assignment (PD group, HE group, and HY group) and five time points from the acquisition and retention phases. These were 1) Baseline Block trials (No Stim), 2) Acquisition Block-1 stimulation trials (EARLY), 3) Acquisition Block-3 stimulation trials (MID), 4) Acquisition Block-5 stimulation trials (LATE), and 5) Retention Block-2 stimulation trials (RET). The middle block of trials during retention was chosen to avoid transient motor learning factors such as warm-up decrement and fatigue from artificially influencing subject performance.[26] Six dependent variables of interest were considered to assess the influence of the independent variables on postural control, postural coordination, and base of support

(BOS) transition.

Perturbation recovery time measured the time between tether release and cessation of center of mass (COM) movement posteriorly (COM stop). This variable served to assess overall postural control. Shorter recovery times were interpreted as better postural control as these could represent either or both: 1) fewer rearward steps being taken and 2) a shorter interval to reverse the trajectory of the COM from backward (ie, compensatory response) to forward (ie, volitional response).

Postural coordination was assessed using three variables: the ratio of COM position change to step length (COM:SL ratio), peak COM velocity, and peak knee flexion. The COM:SL ratio was calculated as the ratio of COM displacement between tether release and foot strike of the swing limb during the first step of the compensatory stepping response to the length of that step. A greater COM:SL ratio was interpreted as poorer postural coordination, as this indicated that the COM was allowed to travel a greater distance posteriorly with respect to the change in the base of support during the compensatory response. Peak COM velocity was calculated as the maximum rate of change in the COM between tether release and COM stop. COM velocity was specifically considered in context to its change over time, such that either remaining constant or decreasing were interpreted as beneficial to postural coordination as this indicated that subjects were either automatically or volitionally constraining rearward COM displacement during the compensatory step. Peak knee flexion was calculated as the maximal amount of swing limb knee flexion attained between the point at which the foot left the ground (foot off) to the point at which it contacted the ground again (foot strike) during the first compensatory step. Less knee flexion was interpreted as poorer

postural coordination as it allowed less clearance of the swing limb during BOS transition.

Two variables were used to assess BOS transition. These were total hip motion and step length. Total hip motion was calculated as the integral of the rectified velocity of the hip from foot off to foot strike during the first compensatory step. Greater hip motion was interpreted as being beneficial to effectively transitioning the BOS, while less hip motion was interpreted as being indicative of a hypokinetic response to the loss of balance. Step length was calculated as the vector distance (it accounted for sagittal and frontal plane movement) the swing limb travelled between tether release and foot strike of the first compensatory step. Greater step length was interpreted as being beneficial to successful BOS transition, while smaller step length was interpreted as a hypokinetic BOS transition.

Each variable was compared across five time points as outlined previously using blocked averages from three consecutive trials. The block of non-GVS trials (No-Stim) was compared to Early, Mid, and Late blocks of GVS trials during the acquisition phase to identify within session adaptation in performance that may have occurred with exposure to repeated sensory illusions. The No-Stim block was also compared to the retention block to determine if adaptation was persistent.

Data were analyzed using separate, 3x5 mixed model analyses of variance (ANOVA) with repeated measures on the time factor. In the event of a significant finding in the omnibus F tests, post-hoc tests were performed using Bonferroni correction to correct for multiple comparisons of main effects between and within subjects. The initial level of significance for all comparisons was set at 0.05. All statistical analyses were

performed with SPSS 19 (IBM Inc; Armonk, NY,USA). Effect sizes were calculated to assess standardized mean differences between groups and across time. To control for inflation of the effect size due to a small sample size, Hedge's g was calculated for between group differences (annotated hereafter as g_s) and within group differences across time (annotated hereafter as g_{av}) in accordance with the guidelines reviewed by Lakens et al.[27] Hedge's g is a corollary of Cohen's d, used for small sample sizes, and as such ranges from 0 to infinity and is interpreted as a percentage of the standard deviation (ie, $g_s = 0.5$ means the effect size is half the standard deviation). In order to simplify interpretation of the effect sizes, we also calculated the common language effect size (CL). The CL is expressed as a percentage and expresses the likelihood that an individual from one group (or measurement from one time point) will differ from an individual from another group (or measurement from another time point).[27]

Results

Twenty-seven individuals with PD, 22 healthy elderly adults and 17 healthy young adults were screened for inclusion in this study. Among individuals with PD who were excluded from the study, three had had surgery for their PD symptoms, four had a comorbid peripheral neuropathy, and eight had a Hoehn & Yahr score greater than III. Eleven elderly adults were excluded from participation due to recent orthopedic surgery (n = 3), peripheral neuropathy (n = 5), and severe arthritis (n = 3). Two young adults were excluded from the study due to recent orthopedic injuries that affected their balance. Thirty-five participants completed testing. Data for one individual in the HE group were corrupted and unable to be used for analysis. Therefore, analyses were performed on 34 participants. Participant characteristics are presented in Table 4.1.

Table 4.1: Participant Characteristics (N = 37)

	HY (N = 15) $\overline{x}$ (95% CI)	PD (N = 12) $\overline{x}$ (95% CI)	HE (N = 10) $\overline{x}$ (95% CI)
Age (yrs)	25.6 (24.4-26.8)	70.5 (65.0-75.9)	63.6 (56.9-70.3)
Hgt(cm)	172.9 (166.3-179.4)	172.6 (167.2-177.9)	174.5 (170.6-178.3)
Wgt(kg)	74.7 (62.9-86.4)	80.8 (74.4-87.1)	91.4 (77.9-104.8)
FGA	--- NA ---	23.9 (21.7-26.2)	27.9 (26.3-29.5)
UPDRS	--- NA ---	18.3 (13.1-23.4)	--- NA ---

FGA – Functional Gait Assessment
UPDRS – Motor Subcomponent of Movement Disorders Society Unified Parkinson Disease Rating Scale

Postural Control

There was not an interaction effect or a main effect for time for perturbation recovery time (Figure 4.1), which suggests that repeated exposure to GVS did not influence recovery time for any group. Within group effect size comparisons support this observation. Effect sizes were generally small when comparing the nonstimulated condition to each acquisition and retention block, CL values for these comparisons never rose above 62% at any time point for any group (Table 4.2). There was a significant group effect for perturbation recovery time ($F = 3.9$, $df = 2$, $p = .029$). Post-hoc testing demonstrated that the PD group took longer to recover from the posterior loss of balance than the HY group ($p = .043$; Table 4.3). There was not a significant difference between the PD and HE groups, and effect sizes were small ($g_s = .14$, CL = 54%). Effect sizes comparing the HY group to the PD and HE groups were large ($g_s = .98$ and .83, respectively). The between group CL effect sizes showed that the likelihood that someone from the HY group would have a shorter recovery time than someone from the PD group was 76%. This likelihood was 73% when comparing individuals in the HY and HE groups, despite a lack of statistical significance between these two groups (Table 4.3).

Postural Coordination

There was a significant interaction effect for peak COM velocity ($F = 3.2$, $df = 5.7$, $p = .008$; Figure 4.2). Post-hoc comparisons demonstrated that in the PD group compared to the nonstimulated trial block ($\overline{x} = .70$, SD = .12), peak velocity significantly decreased at the midpoint of acquisition ($\overline{x} = .56$, SD = .14, $p = .001$) and at retention ($\overline{x} = .55$, SD = .16, $p = .002$). A similar effect was not seen in the control groups. Within group effect sizes (Hedge's g_{av}) in the PD group comparing the nonstimulated trial block

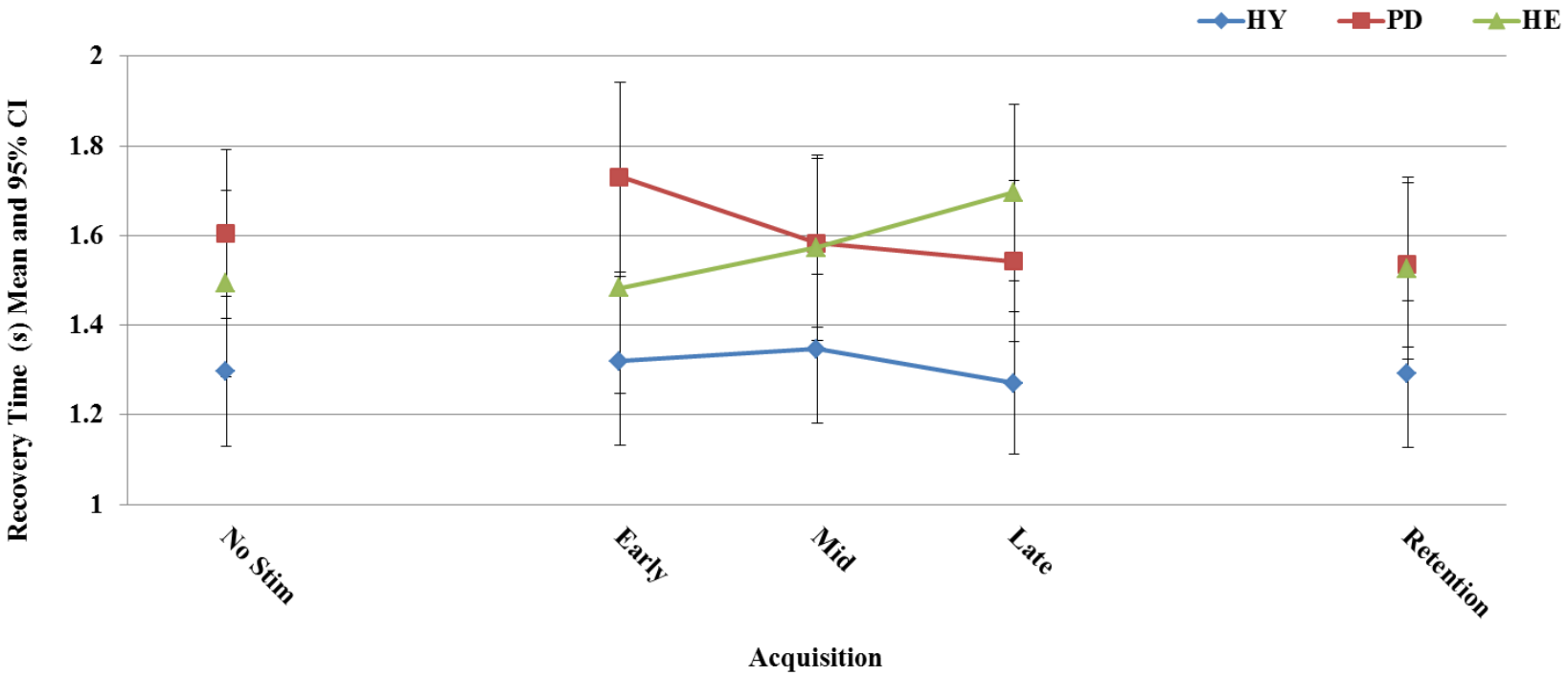

Figure 4.1: Average Group Perturbation Recovery Times (s) at Prestimulation, Acquisition, and Retention

Table 4.2: Effect Size Indices Comparing Baseline (No Stim) Block to Acquisition and Retention Blocks

	Acquisition						Retention	
	Early		Mid		Late			
HY	g_s	CL	g_s	CL	g_s	CL	g_s	CL
Perturbation Recovery	.02	51%	.09	55%	.16	58%	.03	52%
Peak COM Velocity	.09	55%	.15	57%	.40	74%	.25	60%
COM:SL ratio	.50	64%	.51	64%	.51	64%	.53	66%
Peak Knee Flexion	.30	60%	.58	70%	.72	72%	.39	62%
Total Hip Displacement	.34	63%	.61	72%	.82	80%	.22	59%
Step Length	.04	52%	.10	54%	.03	51%	.24	60%
PD								
Perturbation Recovery	.32	60%	.06	52%	.18	58%	.20	58%
Peak COM Velocity	.21	59%	.95	89%	.71	75%	1.03	85%
COM:SL ratio	.72	79%	.88	75%	.79	82%	.99	79%
Peak Knee Flexion	.03	52%	.06	53%	.03	51%	.04	52%
Total Hip Displacement	.02	52%	.33	61%	.36	60%	.07	53%
Step Length	.13	59%	.13	57%	.11	56%	.10	55%
HE								
Perturbation Recovery	.22	60%	.28	61%	.38	62%	.23	57%
Peak COM Velocity	.05	51%	.04	51%	.49	63%	.23	60%
COM:SL ratio	.80	79%	.33	60%	.16	54%	1.05	85%
Peak Knee Flexion	.19	56%	.16	55%	.35	62%	.17	58%
Total Hip Displacement	.46	63%	.46	66%	1.01	77%	.83	68%
Step Length	.08	55%	.03	54%	0	50%	.09	55%

g_{av} Hedges g effect size index CL Common Language effect size index

Table 4.3: Between Group Comparisons and Effect Size Indices

	HY	PD	HE	HY:PD		HE:PD		HY:HE	
	$\overline{x}$ (95% CI)	$\overline{x}$ (95% CI)	$\overline{x}$ (95% CI)	g_s	CL	g_s	CL	g_s	CL
Perturbation Recovery (s)*	**1.31(1.15-1.46)**	1.60 (1.43-1.77)	1.56 (1.36-1.75)	.98	76%	.14	54%	.83	73%
Peak COM Velocity (m/s)*	**.79 (.71-.85)**	.61 (.53-69)	**.80 (.71-.89)**	1.22	81%	1.37	84%	.16	55%
COM:SL ratio	.27 (.21-34)	.36 (.29-44)	.28 (.20-.36)	.69	69%	.62	68%	.07	52%
Peak Knee Flexion (deg)*	**62.2 (58.4-66.0)**	38.8 (34.5-43.1)	**49.6 (44.9-54.3)**	3.13	99%	1.43	85%	1.68	89%
Total Hip Displacement*	**36.3 (30.2-42.5)**	23.2 (16.3-30.1)	30.9 (23.4-38.6)	1.08	78%	.63	68%	.44	63%
Step Length (m)*	**.31 (.28-.34)**	.16 (.12-.19)	**.29 (.25-.33)**	2.46	96%	2.22	95%	.25	57%

* significant group main effect, post-hoc difference from PD group is in in **BOLD,** post-hoc difference from HE group is Underlined

$\overline{x}$ Mean

CI confidence interval

gs Hedges g between group effect size index

CL Common Language effect size index

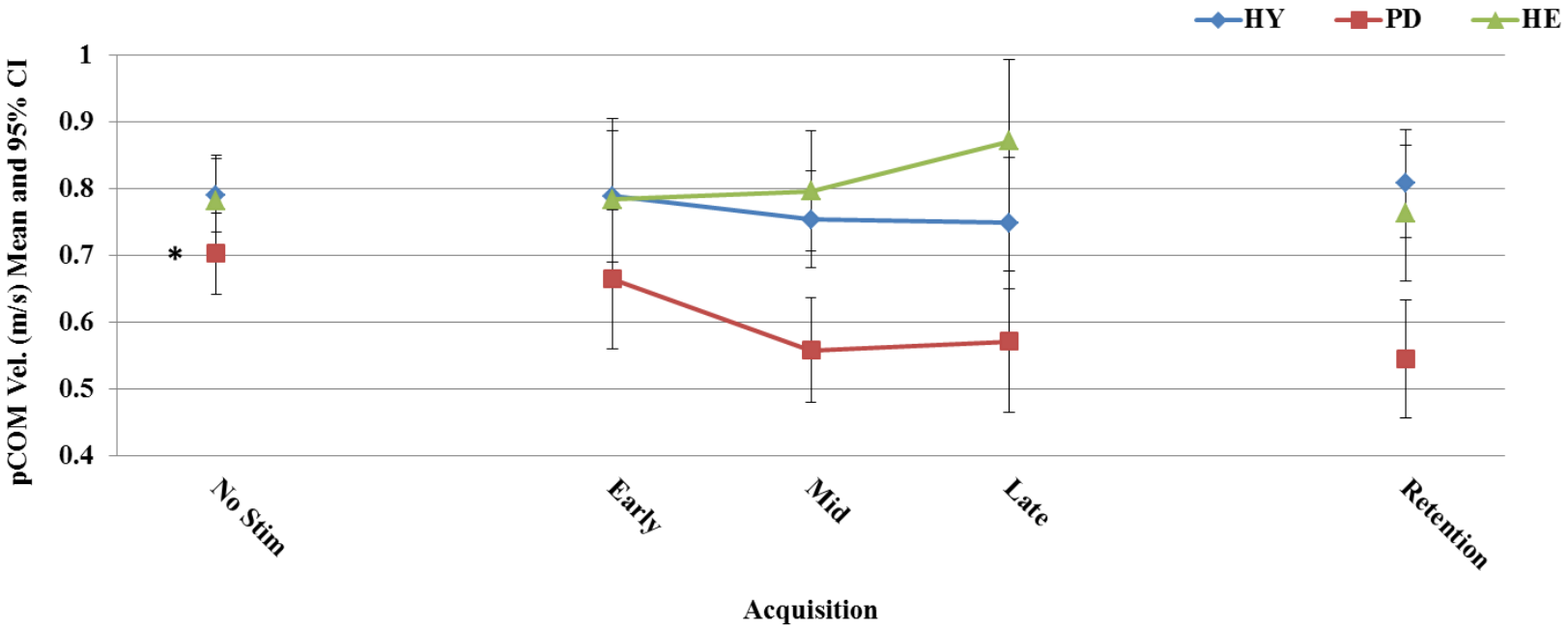

Figure 4.2: Average Group Peak COM Velocity (m/s) at Prestimulation, Acquisition, and Retention
* Significant decrease in velocity at Mid / Late Acquisition and Retention in PD Group

to acquisition and retention blocks were large in Mid, Late, and Ret blocks, ranging from .71-1.03, with corresponding CL effect sizes ranging from 75%-89%. Effect sizes for the HY and HE groups were substantially lower (Table 4.2). These findings indicate that individuals in the PD group constrained COM movement during repeated GVS exposure. There was also a significant group effect (F = 7.4, df = 2, p = .002). Post-hoc comparisons showed the peak COM velocity in the PD group ($\overline{x}$ = .61, SD = .13) was significantly lower than the HY ($\overline{x}$ = .79, SD = .14, p = .007, g_s = 1.22, CL = 81%) and HE ($\overline{x}$ = .80, SD = .14, p = .007, g_s = 1.37, CL = 84%) groups (Table 4.3). There was not a significant time effect.

There was a significant interaction effect for COM:SL ratio (F = 3.9, df = 3.2, p = .012; Figure 4.3). Post-hoc comparisons demonstrated that compared to the nonstimulated trial block ($\overline{x}$ = .59, SD = .28), the COM:SL ratio was significantly lower at Early ($\overline{x}$ = .35, SD = .11, p = .001 g_s = .72, CL = 79%), Mid ($\overline{x}$ = .31, SD = .10, p = .006, g_s = .88, CL = 75%), Late ($\overline{x}$ = .30, SD = .15, p < .001, g_s = .79, CL = 82%), and Retention testing ($\overline{x}$ = .28, SD = .09, p = .001, g_s = .99, CL = 79%) in the PD group, but not in other groups despite moderate to large effect sizes in the HE group across time (Table 4.2). There was also a significant time effect (F = 8.2, df = 1.6, p = .002), which may be attributable to the effect sizes noted in the PD and HE groups above. There was not a significant group effect and between group effect sizes tended to be moderate (Table 4.3).

There was not an interaction or time effect for peak knee flexion (Figure 4.4). Within group effect sizes comparing the nonstimulated trial block to acquisition and retention blocks for peak knee flexion tended to be small to moderate and did not change

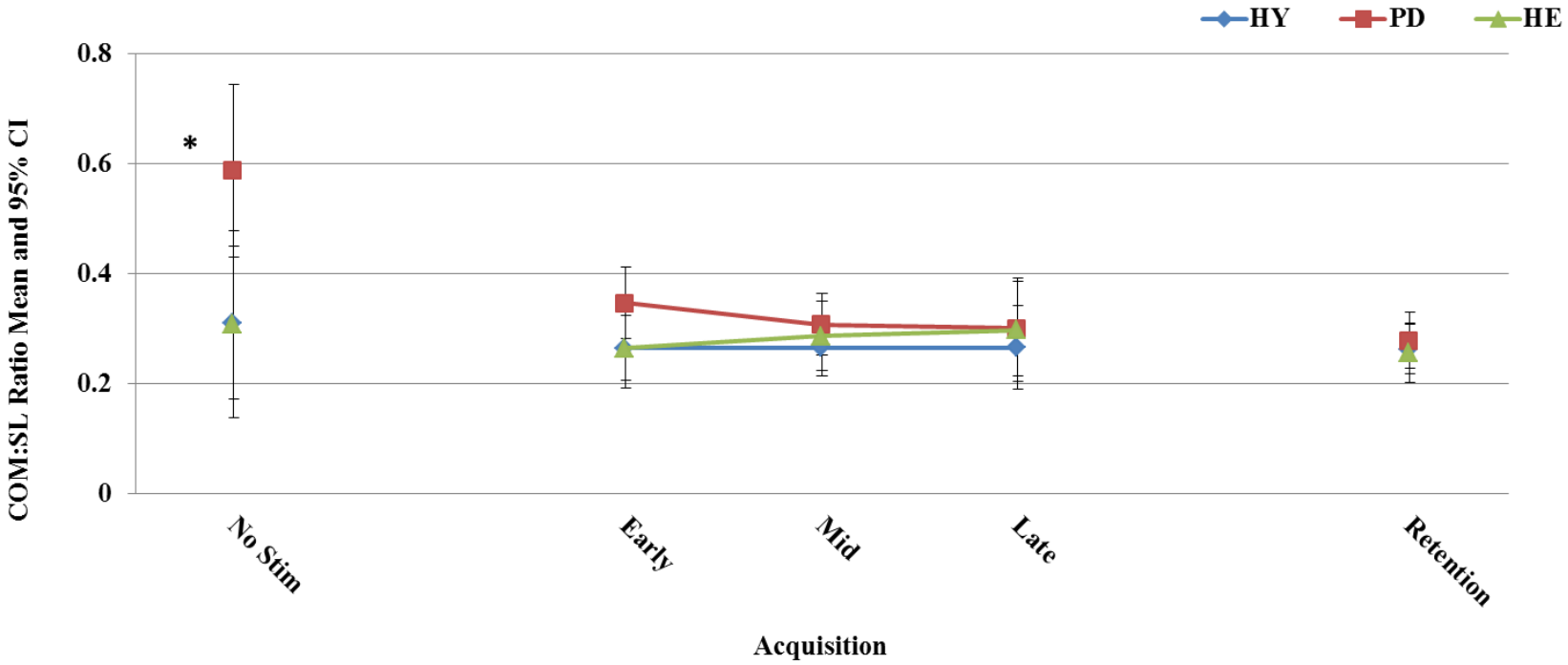

Figure 4.3: Average Group COM:SL Ratio at Prestimulation, Acquisition, and Retention
* Significant decrease in COM:SL Ratio at Acquisition and Retention in PD Group

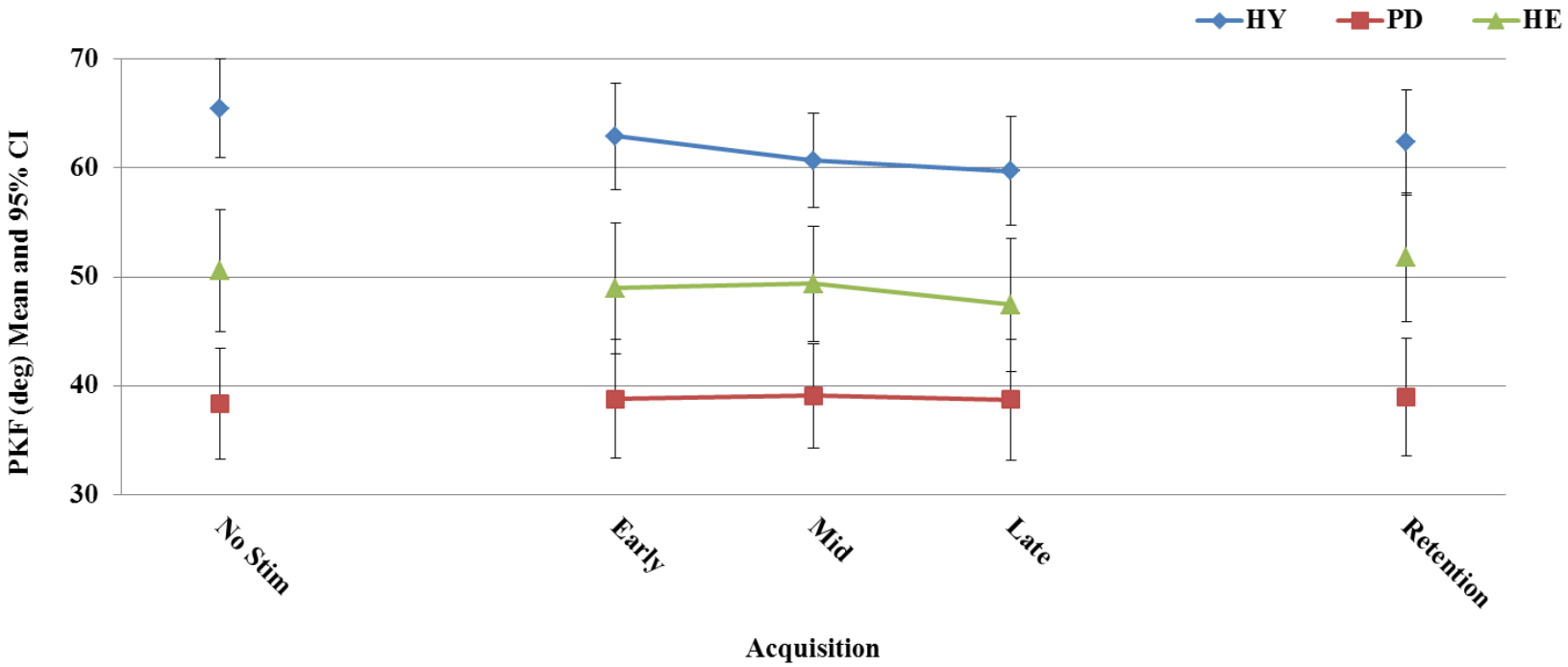

Figure 4.4: Average Group Peak Knee Flexion (deg) at Prestimulation, Acquisition, and Retention

considerably across time (Table 4.2). There was a significant group effect for peak knee flexion (F = 35.0, df = 2, p < .001). Post-hoc comparisons (Table 4.3) showed that the PD group had markedly less peak knee flexion ($\overline{x}$ = 38.8, SD = 7.3), than the HY ($\overline{x}$ = 62.23, SD = 7.26, p < .001, g_s = 3.13, CL = 99%) and HE ($\overline{x}$ = 49.64, SD = 7.28, p < .001, g_s = 1.43, CL = 85%) groups. The HE group also had significantly less knee flexion than the HY group (p < .001, g_s = 1.68, CL = 89%).

BOS Transition

We observed no interaction or time effects for total hip displacement (Figure 4.5). Additionally, within group effect sizes comparing the nonstimulated trial block to acquisition and retention blocks tended to be small to moderate and did not change considerably across time (Table 4.2). There was a significant group effect for total hip displacement (F = 4.1, df = 2, p = .025). Post-hoc comparisons (Table 4.3) demonstrated that the PD group ($\overline{x}$ = 23.24, SD = 11.8 degrees) had significantly less hip excursion than the HY group ($\overline{x}$ = 36.34, SD = 11.79, p < .021, g_s = 1.08, CL = 78%), but did not differ from the HE group ($\overline{x}$ = 30.99, SD = 11.78, p > .05, g_s = .63, CL = 68%). There was also no difference between the HE and HY groups (p > .05, g_s = .44, CL = 63%).

There were no interaction or time effects for step length and within group effect sizes comparing the nonstimulated trial block to acquisition, and retention blocks tended to be small and did not change considerably across time (Figure 4.6; Table 4.2). There was a significant group effect for step length (F = 21.5, df = 2, p < .001). Post-hoc comparisons (Table 4.3) demonstrated that the PD group ($\overline{x}$ = .16 m, SD = .07 m) had a significantly smaller compensatory step than the HY group ($\overline{x}$ = .31 m, SD = .05 m, p < .001, g_s = 2.46, CL = 96%), and the HE group ($\overline{x}$ = .29, SD = .06, p < .001, g_s = 2.22,

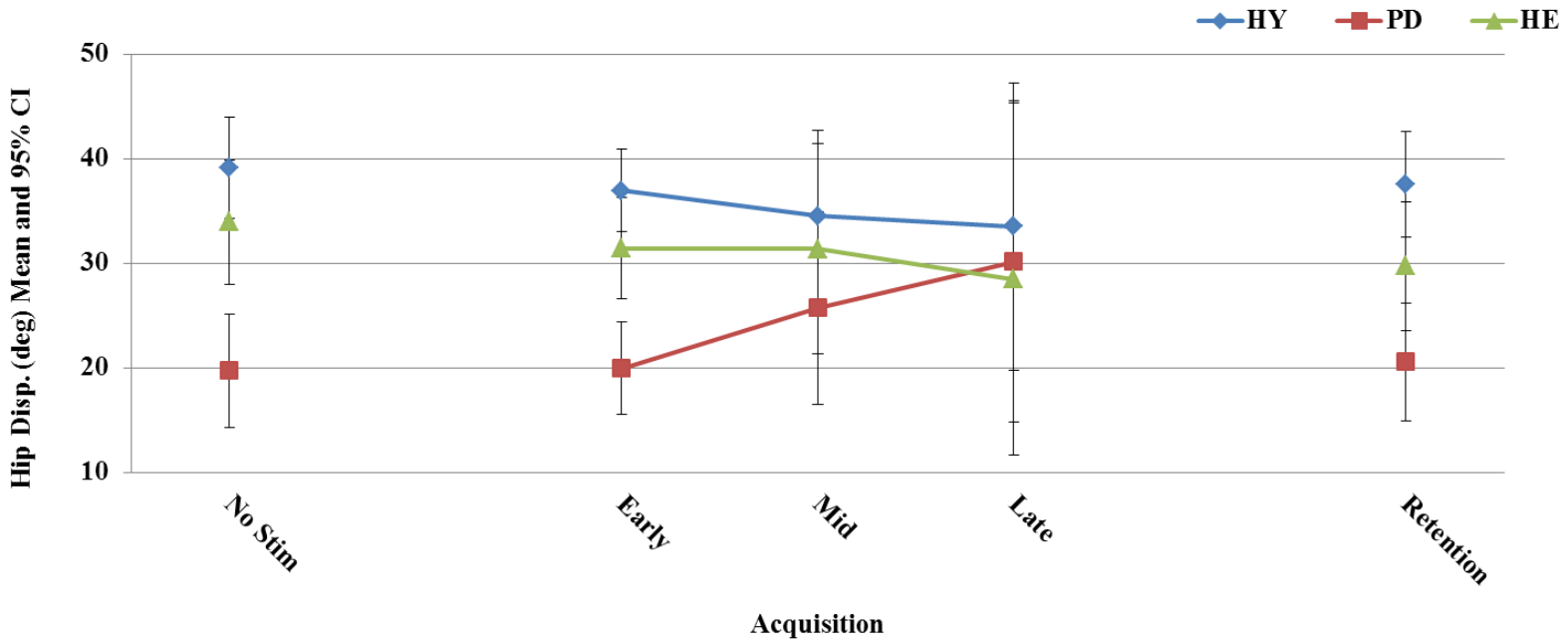

Figure 4.5: Average Group Total Hip Displacement (deg) at Prestimulation, Acquisition, and Retention

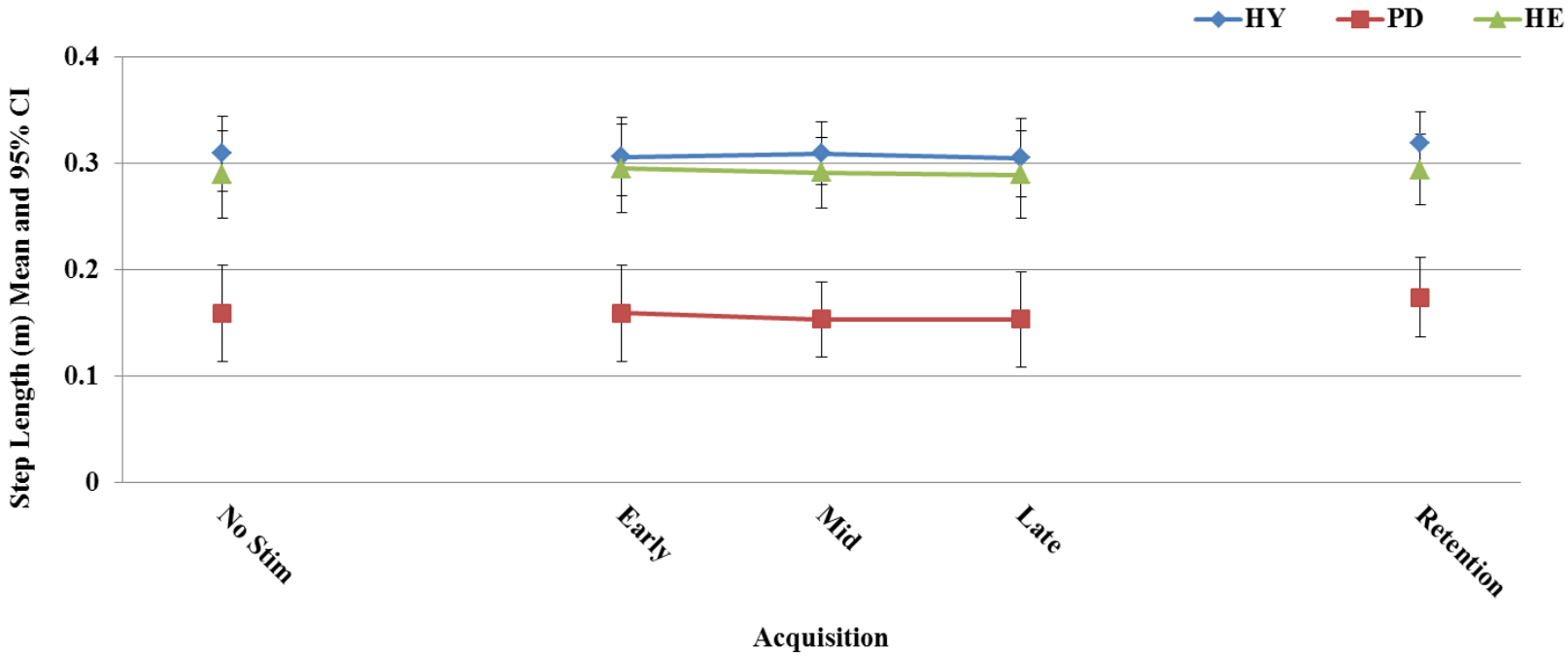

Figure 4.6: Average Group Step Length (m) at Prestimulation, Acquisition, and Retention

CL = 95%). There was no difference between the HE and HY groups ($p > .05$, $g_s = .25$, CL = 57%).

Discussion

In this study we sought to determine whether repeated exposure to a vestibular sensory illusion evoked by GVS would influence postural responses in healthy young adults, healthy older adults, and individuals with Parkinson disease. We hypothesized that initial exposure to a sensory illusion would result in a deterioration of performance across groups relative to an unstimulated trial, but that repeated exposure to the illusion would result in adaptation to the vestibular illusion and postural measures would approximate or improve over nonstimulated levels. We further hypothesized that individuals with PD would demonstrate hypokinetic and bradykinetic postural responses to an unexpected posterior loss of balance in comparison to controls. To meet this end, we employed a classic motor learning paradigm in which subjects underwent a series of practice trials on one day followed by a smaller series of trials on a subsequent day. In contrast to our primary hypothesis, little improvement was seen on the majority of outcomes across groups following repeated exposure to the sensory illusion, which may indicate that the intensity or timing of the vestibular illusion used in this study was insufficient to influence the stepping response. Alternatively, the larger perturbation caused by the tether release and the stereotyped task that it provokes was insensitive to the GVS illusion. In support of our secondary hypothesis, individuals with PD did demonstrate a paucity and / or slowness of movement during compensatory stepping in response to a posterior loss of balance.

Acute and Adaptive Effects of GVS Exposure on Postural Responses Following Tether Release

We found that acute and repeated exposure to GVS immediately preceding tether release failed to exert substantial influence on postural control in individuals with PD or either control group. Acute GVS exposure also did not impact factors associated with the transition of the BOS. However, the COM:SL ratio decreased significantly from the nonstimulated trial block to early acquisition in the PD group. There was a similar trend in peak COM velocity, which reached significance when comparing the nonstimulated trial block to later acquisition blocks. These changes persisted following early acquisition. In the PD group, repeated GVS exposure was also associated with an adaptive trend in BOS transition, specifically a moderate, though nonsignificant trend of increased hip extension from early to late acquisition. Additionally, individuals in the PD group demonstrated acute and adaptive postural coordination responses. The combination of the decreased COM:SL ratio, lower COM velocity, and transiently increased hip extension suggest that individuals with PD may have developed a protective strategy to accommodate a smaller step length in light of the impending threat to posterior balance loss. Since prestimulation kinematic and kinetic data did not show a greater forward lean in these subjects through acquisition or retention trials, and there was not a premature decrease in force against the tether load cell prior to tether release, this protective response coincided with or rapidly followed GVS. We believe that individuals with PD may have used the GVS as a sensory cue to produce a compensatory trunk adjustment (slight forward lean). This would account for the decrease in COM velocity and position change as well as the increase in hip extension and would provide

some accommodation for the reduced step length observed in these subjects. Postural strategy selection and execution in response to a perturbation are known to be influenced by prior experience.[28] Given that posterior postural stability is diminished in PD, these individuals likely experienced a greater postural threat to the tether release than did controls.[29] The increased threat, in turn, may have provoked the compensation we observed in these subjects. Previous research investigating quiet stance responses to increases in postural threat has shown alterations of postural strategies are used to minimize a perceived threat.[30]

Influence of PD and Age on Postural Responses Following Tether Release

Individuals with PD demonstrated diminished postural control as evidenced by increased recovery time. We also observed a decrease in postural coordination in individuals with PD demonstrated by lower COM velocity and reduced knee flexion of the stepping limb. There was also marked reduction in BOS transition among individuals with PD, specifically reduced hip displacement and a shorter step length. Previous reports have also shown that individuals with PD have greater difficulty than controls with postural control, coordination and BOS transition in response to both forward and backward loss of balance.[17,18,31,32] Taken together, our data serve to extend previous research showing that slowness and paucity of movement associated with PD negatively influence compensatory stepping in response to posterior perturbations.

Postural control was statistically similar between healthy young and older adults, though the CL effect size index indicated that there is a 73% likelihood that recovery from an unexpected posterior loss of balance is longer in older healthy individuals (Table

4.3). This suggests that there is degradation in postural stability associated with aging to sudden, unexpected perturbations. Previous research[33,34] has shown that older individuals are less stable in response to a slip perturbation, but that stability improves with training.[33] We failed to see an improvement in postural stability with repeated tether release in our older subjects. This may indicate that a longer training period is needed to evoke an adaptive response, or that GVS acts as a distractor in older subjects and impairs adaptation to a reactive postural task with a high threat level. We also observed differences in postural coordination, specifically swing limb peak knee flexion which influenced limb clearance during stepping. Similar findings following a forward loss of balance have previously been reported.[35] Healthy young and older adults tended to perform similarly across other measures of postural coordination and BOS transition in response to tether release. Previous research has also demonstrated COM velocity and step length do not differ with age to forward or backward balance perturbations.[36-38] Taken together, our findings indicate that young and older healthy adults have initial compensatory steps that are similar in speed and magnitude, but differ in limb clearance length of time to recover postural control. The decreased limb clearance and longer recovery time of the older healthy adults may indicate that the stepping limb is less efficient in slowing the COM after foot strike of the initial compensatory step, resulting in continued posterior displacement of the COM and the need for multiple steps to stop the body's momentum.

Limitations and Future Research

We were not able to definitively determine whether the acute and adaptive postural changes we observed occurred as a result of GVS exposure or exposure to

repeated tether release trials, though it seems likely it was the latter's influence. Osler et al.[39] reported that GVS evoked similar sway patterns in subjects with their eyes closed when standing on a narrow walkway at ground level and when placed 4 m above the ground. However, postural sway was severely attenuated in the latter condition within 800 ms. This suggests that effects of GVS are suppressed when postural threat is heightened as was the case in our study. Future research should examine differences in the adaptation of postural responses when the tether release is applied independently and combined with GVS to determine whether effects may be additive.

In addition to the difficulty of delineating GVS and tether effects in the current study, there appeared to be little influence of GVS on compensatory stepping. This may have occurred due to the rapid linear acceleration of the COM backwards following tether release, which would also stimulate a vestibular response subsequent to the sensory illusion[40] as well as visual and proprioceptive responses due to changes in optic flow[41] and joint angular changes.[42] Additionally, GVS may have been temporally ineffective (eg, insufficient duration, ill-timed latency) to evoke the desired response. Stimulation in the current study ended within 300 ms of tether release, which may have been too early to influence later components of the stepping response. Future research should investigate the influence of repeated exposure to posterior tether release across age groups and in healthy versus balance impaired populations over longer time periods and various dosage applications to determine thresholds for motor learning in these populations. Additionally, future research should investigate whether longer duration GVS, which occurs simultaneously with the landing phase of the stepping response influences postural reactions.

Age matching was imperfect in the current study, which potentially limited our ability to discern between age-related and PD-related differences in postural control following acute or repeated GVS application. In order to mitigate this weakness in our study we conducted separate ANCOVAs for each variable of interest, comparing individuals with PD and healthy elders using age as a covariate. Results of these analyses did not differ from results of similarly conducted ANOVAs comparing these groups. Therefore, we believe age did not confound our results and our interpretation of differences attributed to age or PD are correct. Future research should seek to confirm our findings in a larger cohort of individuals with PD and healthy elders using a tighter restriction on age-matching.

Conclusion

Individuals with PD show marked deficits in postural responses to an unexpected, evoked posterior loss of balance coupled with a vestibular sensory illusion compared to healthy young and age-matched controls. Certain biomechanical components of postural stability appear to be amenable to change with repeated perturbation exposure. These finding should assist clinicians in developing balance training programs to address posterior postural instability.

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CHAPTER 5

GENERAL DISCUSSION

Postural instability is one of the cardinal signs of Parkinson disease (PD) and is among the leading factors of morbidity and mortality associated with the disease due to its linkage with injurious falls in this population.[1-3] Postural instability is linked to deficits in sensory integration in this population, but little is still understood about the ability of individuals with PD to develop adaptive postural responses to rapid changes in the sensory environment with practice.[4-8] Additionally, the ability of these individuals to develop such adaptive strategies across a spectrum of postural tasks has not been fully elucidated. The work in this dissertation was therefore undertaken to gain a better understanding of whether individuals with PD were able to develop adaptive postural responses to vestibular sensory illusions during static, anticipatory and reactive postural tasks on a level commensurate with healthy controls.

We began by undertaking a study to determine whether PD or age would differentially affect acute postural recovery or adaptive postural responses to novel or repeated exposure to a vestibular sensory illusion using GVS during a static postural task. In addition, we sought to determine the time course of postural recovery following a vestibular sensory across groups. Results of this study demonstrated that postural instability increased within a trial across all groups following application of GVS, but individuals with PD had a diminished capacity to stabilize their COP acutely following

sensory illusion compared to other groups and that this diminished capacity was related to a decrease in complexity of the motor output of the postural control system in these individuals and in age-matched controls. We further found that neither individuals with PD or healthy older adults showed increases in the complexity of postural control system motor output nor did they demonstrate clinically meaningful improvements in postural control with repeated exposure to the vestibular illusion either during acquisition or during retention testing following a 48-hour period allowing for consolidation. In contrast, healthy young adults acutely changed their postural control behavior to the novel sensory illusion (by acutely changing from high to low system complexity). This response persisted through acquisition; however, following a period of consolidation, complexity of system output increased in this group, which coincided with a clinically meaningful improvement in postural stability. Taken together, these results suggest that young adults may have been able to develop an exploratory strategy in order to learn to adapt to the sensory illusion, while older adults and those with PD were not. Further investigation in future studies in order to determine the veracity of this possibility is warranted.

We also sought to determine the influence of GVS-induced sensory illusions on postural control of an anticipatory task. Therefore, we conducted a second study to assess the influence of novel and repeated exposure to GVS on postural responses associated with an anticipatory postural task to determine if age and PD differentially affect acute or adaptive postural responses relevant to the task. We hypothesized that initial exposure to a sensory illusion would result in a deterioration of performance across groups, but that repeated exposure to the illusion would produce a central nervous system

mediated suppression of vestibular input that would result in improved performance. Results of this study demonstrated that acute exposure to GVS resulted in impaired motor planning, a small but potentially meaningful abberation in postural preparation, and decreased postural stability in the PD group, while healthy controls demonstrated an ability to effectively suppress and leverage exposure to an acute sensory illusion by using GVS as a cue to perform the RTT task. We further found that with repeated exposure to GVS, individuals with PD learned to suppress the sensory illusion, thereby improving motor planning, restoring normal postural preparation, and improving postural stability at later acquisition and retention time points compared to early acquistion. Taken together, these findings indicate that the ability to reweight sensory stimuli to improve postural control is impaired, but present in individuals with PD. Additionally, our findings suggest that the healthy nervous system rapidly suppresses vestibular illusions when performing a voluntary postural task that requires a planned change or reduction in the BOS. In this context the CNS may rely more heavily on somatosensory or visual information to meet the objectives of the task.

In order to evaluate a spectrum of postural control scenarios, we also undertook a study to determine whether repeated exposure to a vestibular sensory illusion that was coupled with a reactive postural control task would differentially influence acute or adaptive postural responses in healthy young adults, healthy older adults, and individuals with Parkinson disease. We hypothesized that initial exposure to a sensory illusion would result in a deterioration of performance across groups relative to an unstimulated trial, but that repeated exposure to the illusion would result in adaptation to the vestibular illusion and postural measures would approximate or improve over nonstimulated levels. Results

from this study showed that in individuals with PD measures of postural coordination decreased with acute exposure to GVS, while postural control and BOS transition were unaffected initially. Repeated exposure to GVS in these individuals demonstrated persistent adaptive changes in postural coordination and an adaptive trend in BOS transition. Taken together, it appeared that persons with PD developed a protective strategy to accommodate a smaller step length in light of the impending threat to posterior balance loss that coincided with or rapidly followed GVS. We believe, given that posterior postural stability is diminished in PD, these individuals likely experienced a greater postural threat to the tether release than did controls.[9] The increased threat, in turn, may have provoked the compensation we observed in these subjects.

As stated in the introduction of this dissertation work, our principle goal was to determine the influence of acute and repeated exposure to vestibular sensory illusions on sensory reweighting and to lay the groundwork toward developing evidence-based sensorimotor adaptation paradigms to improve postural control in PD. Such paradigms are necessary because few, if any, existing initiatives integrate sensory and motor perturbations into balance training in this population. Integrated training should produce more functional sensorimotor adaptations to postural threats, but to date this hypothesis has not been rigorously studied. Findings from the current work lend support to this hypothesis and highlight the need for specific research initiatives that would facilitate the development of these types of clinical programs.

Based on our results, individuals with PD appear to have an intact, albeit impaired, ability to learn to reweight aberrant sensory stimuli that conflict with information from other postural control related senses. This suggests that incorporation

of training regimens that employ sensory reweighting is warranted. Future research should investigate the use of a broader spectrum of sensory reweighting paradigms to identify those most amenable to clinical practice in this and other neurologically impaired populations.

Our results also suggest that physiologic changes associated with aging and PD may blunt adaptive responses in these individuals. Therefore, it may be necessary to provide a greater level of exposure to sensory reweighting paradigms either through massed practice or through a greater number of training intervals to promote adaptation in these individuals. Future research should evaluate appropriate types and levels of training necessary to produce the most robust adaptive responses in order to determine their feasibility in a clinical setting.

Furthermore, our results seem to indicate that depending on the level of postural threat associated with a balance challenge, individuals with PD may produce protective strategies to minimize their immediate risk of balance loss (such as that seen during tether release discussed in Chapter 4). Such strategies may not capitalize on the most appropriate means of postural recovery. Specifically, individuals with PD may attempt to reduce their freedom of movement (ie, by cocontracting lower extremity muscles or stiffening their joints) to influence their center of mass movement, rather than taking a larger step to arrest their movement as they approach their postural stability limits. Future research should attempt to measure and correct this type of activity through the use of appropriate task constraints or biofeedback.

Taken together, results of these studies demonstrated that acute exposure to a vestibular sensory illusion differentially affects postural control in individuals with PD.

Our results lend further support to the hypothesis that reweighting of sensory stimuli is impaired as a result of PD. However, our results also indicate that individuals with PD are able to suppress attention to a vestibular illusion and demonstrate adaptive responses to a postural threat.

Limitations and Future Research

Findings associated with the studies reported in this dissertation contribute to the understanding of the influence of sensory reweighting on aspects of postural control in individuals with PD. However, this work was limited by a number of factors. One limitation we encountered was providing an appropriate intensity and duration of the sensory illusion to produce a compensatory postural response across all tasks and conditions studied. Specifically, we were unable to determine if the applied GVS adequately influenced postural responses during the tether release task. Because this task produces such a large and robust multisensory response independent of any sensory manipulation, future research should consider either evaluating the influence of sensory illusions on a less challenging reactive task or comparing the task alone to single and multisensory illusions in order to evaluate the influence of sensory reweighting on this type of task.

An additional limitation of this series of studies was incorporation of an appropriate number of practice sessions to allow skill adaptation to occur across subject groups. It is possible that additional training sessions would have produced adaptive responses to sensory illusions in individuals with PD and healthy elders, particularly during quiet stance. Future research should compare single to multisession training of sensory illusions to determine if individuals with PD and healthy elders require a greater

threshold of training to produce adaptive responses.

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