Balance Function: A Potential Early Indicator of Mild Cognitive Impairment

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Balance Function: A Potential Early Indicator of Mild Cognitive Impairment

by

Karen L. Bell

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy with a concentration in Neurocommunicative Science Department of Communication Sciences and Disorders College of Behavioral and Community Sciences University of South Florida

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Abstract

This dissertation examined oculomotor and vestibular function, functional balance and spatial ability in young adults, cognitively normal older adults (CNOA), and older adults with MCI. Oculomotor and vestibular function were assessed using videonystagmography (VNG), vestibular evoked myogenic potentials (VEMPs), the modified Clinical Test of Sensory Integration and Balance (mCTSIB), and the Fukuda Stepping test. Functional balance was assessed using the Timed Up and Go (Podsiadlo & Richardson, 1991) and Functional Reach tests (Duncan et al., 1990). Spatial ability was assessed using the Hidden Goal Task (Kalová et al., 2005), a computerized test of spatial navigation. Forty-two participants comprised three groups (young adults, n = 15; CNOA, n = 13; MCI, n = 14). The Montreal Cognitive Assessment ([MoCA]; Nasreddine et al., 2005) was used to assess cognitive status, and a MCI diagnosis was confirmed using standardized neuropsychological testing and a physician’s exam. Two MANOVAs were calculated to: 1) compare young and older adults with and without MCI on oculomotor and vestibular function; and 2) examine group differences on functional balance and spatial ability. Chi-square analysis was calculated to examine the proportion of clinically significant unilateral weakness among groups. Two multiple linear regressions were also calculated to examine the contribution of oculomotor or vestibular function to functional balance and spatial ability. Results indicated the young adult group showed shorter saccade latencies than either CNOA or MCI groups. The MCI group also showed both a higher mean unilateral caloric weakness and a higher occurrence of unilateral caloric weakness than either young adult or CNOA groups. The young adult group showed larger P1-N1 amplitudes than either CNOA or
MCI groups for cervical VEMPs. There were no additional group differences on remaining oculomotor or vestibular measures. The young adult group showed better performance on the Functional Reach and Timed Up and Go tests compared to MCI group, $ps < .005$, however, there were no differences between young adult and CNOA groups, $ps > .114$. The young adult group also showed better performance on the Hidden Goal Task compared to either CNOA or MCI groups, $ps < .042$. Results showed vestibulo-ocular and vestibulo-spinal reflexes were significantly associated with functional balance and spatial ability, respectively. Collectively, these results indicate older adults with MCI may show vestibular asymmetry assessed using bithermal caloric irrigation, however, these findings are not conclusive. These results also suggest vestibulo-ocular and vestibulo-spinal reflex assessment may be considered as part of routine non-invasive battery for detecting signs and symptoms linked to cognitive decline, such as reduced functional balance and spatial ability.
Overall Introduction

Aging is a series of physiological and behavioral changes that occur after an organism achieves full maturity (Shock, 1984). In humans, advancing age is associated with changes in dynamic biological, physiological, environmental, psychological, behavioral, and social processes (National Institute on Aging, 2019). With advancing age, there are expected, universal changes that occur such as changes in physical appearance (e.g., graying hair, skin, and body shape), cognition (e.g., information processing speed, memory), and sensory function (e.g., hearing, vision). Cognitive impairment is not a part of normal aging. Prospective population-based studies show that the prevalence of MCI ranges from 15 – 22% in older adults (Lopez et al., 2003; Petersen, 2009) and have estimated incidence rates of ~ six percent per year (Roberts et al., 2012). The potential of developing cognitive impairment decreases with education and increases with age, doubling approximately every five years above 65 years of age. Changes in physical and cognitive abilities due to dementia onset often leads to limited ability to independently carry out activities of daily living.

MCI is a clinical condition with significant impairment(s) in one or more cognitive domains (e.g., executive function, attention, visuospatial, etc.), in the presence of otherwise everyday functioning, that is not severe enough to warrant a diagnosis of dementia (Petersen, 2004). It is distinct from dementia, which encompasses a larger global impairment with noticeable effects on daily life (Gauthier et al., 2006). Individuals with MCI can carry out activities of daily living with minimal difficulty. Persons with MCI are more likely to progress to
dementia, and approximately 12% of persons with MCI convert to Alzheimer’s disease (AD) per year, a six-fold increase compared to older adults without MCI (Petersen et al., 1999).

By 2030, older adults 65 years and older will represent ~ 21% of the US population, or 74 million people (Federal Interagency Forum on Aging-Related Statistics, 2016). The growth of the older adult population impacts multiple aspects of our global society, presenting challenges to families, businesses, health care providers, and policymakers to meet the needs of aging individuals. As the population of older adults continues to increase, so does the need for enhanced methods and approaches to promote successful aging defined by: 1) low probability of disease and disease-related disability; 2) high cognitive and physical functional capacity; and 3) active social engagement with life (Rowe & Kahn, 1997, 2015). To further understand the processes that contribute to successful aging, research is ongoing to better understand the genetic, environmental, lifestyle, behavioral, and social factors and their influence on aging (Deeg et al., 2018; Halaweh et al., 2018; Martin et al., 2011; Nigam et al., 2012).

It is known that age-related changes in higher-order brain systems result from a reduction in neurotransmitters and alterations in myelinated fibers that connect neurons between cortical regions (Andrews-Hanna et al., 2007; Berger, 2011). Changes in synaptic physiology of aging neurons also contribute to changes in neural connectivity and reduced higher-order integration (Bishop et al., 2010). Functional imaging studies have shown brain regions involved in higher-order cognitive functions (e.g., thinking, perception, planning, and understanding language, etc.) have reduced coordinated activation with age, suggesting a global loss of integrative function; this reduced coordination of brain activity is linked to poor performance in multiple cognitive domains (Andrews-Hanna et al., 2007; Bishop et al., 2010). In addition to reduced integrative function, poor localization of neural activity is associated with age (Cabeza, 2002; Park &
Reuter-Lorenz, 2009). Analysis of genetic and aging model systems suggests that the rate of aging, and cognitive decline of the mammalian brain is variable and open to modification (Bishop et al., 2010). Despite what is known about age-related changes in the brain, the mechanisms of cognitive decline remain unclear. Information processing theory may provide insight into potential mechanisms of cognitive decline (Atkinson & Shiffrin, 1968; Baddeley, 2001; Berger, 2011; Craik & Lockhart, 1972; Leigh & Zee, 2015; Miller, 1956; Morris et al., 1977; Rumelhart et al., 1988). This theory highlights the role of sensory processing in cognitive function suggesting a link between sensory and cognitive processes. Consistent with information processing theory, Albers et al. (2015) report declines in sensory function (e.g., hearing, vision, balance, etc.) occur several years before behavioral signs and symptoms of dementia manifest, and a diagnosis is sought and confirmed. This highlights sensory function as a potential mechanism of cognitive decline and the potential for early detection of cognitive decline by means of sensory function assessment.

Early detection of cognitive decline (i.e., mild cognitive impairment [MCI]) when its symptoms are not visually noticeable, functionally limiting, socially disruptive, or isolating creates an opportunity to delay the progression to dementia. Cognitive screenings and neuropsychological evaluations are common approaches used to detect and characterize cognitive decline. The Montreal Cognitive Assessment ([MoCA]; Nasreddine et al., 2005) is one of the most commonly used and widely accessible cognitive screening tools for detecting cognitive decline with sensitivity and specificity rates of 90% and 87%, respectively. However, the MoCA is often administered when symptoms of decline (e.g., changes in behavior) become noticeable to the individual and/or caregiver. As a critical component of the general healthcare model, primary care and general physicians are positioned to routinely screen older adults for
cognitive decline. However, physicians are unaware of cognitive decline in more than 40% of their patients (Chodosh et al., 2004), and only 16% of older adults report receiving routine cognitive screenings or neuropsychological evaluations (Alzheimer’s Association, 2019). This suggests older adults’ brain health is not routinely assessed or monitored, which directly contributes to delayed detection of cognitive decline. This highlights the need for enhanced approaches to increase early detection of cognitive decline.

Routine sensory function assessment may prove a potential interdisciplinary approach to enhancing early detection of cognitive decline. Clinical tools routinely used to evaluate aspects of sensory function may provide additional evidence of cognitive decline. This would position healthcare specialists who routinely assess domains of sensory function (e.g., audiologist, optometrist, physical therapist, speech-language pathologist, etc.) in older adults to help detect cognitive decline characterized by abnormal changes in sensory function. This dissertation details two pilot studies focused on developing elements of a non-invasive battery aimed to examine balance function as a potential early indicator of MCI. The rationale for completing these studies was to identify elements of a potential balance assessment protocol for use in distinguishing between older adults with and without MCI.
Chapter One: Oculomotor and Vestibular Function in Older Adults with and without Mild Cognitive Impairment

Abstract

This study examined oculomotor and vestibular function in young adults, cognitively normal older adults (CNOA), and older adults with MCI. Oculomotor and vestibular function were assessed using videonystagmography (VNG), vestibular evoked myogenic potentials (VEMPs), the modified Clinical Test of Sensory Integration and Balance (mCTSIB), and the Fukuda Stepping test. Forty-two participants comprised three groups (young adults, n = 15; CNOA, n = 13; MCI, n = 14). The Montreal Cognitive Assessment ([MoCA]; Nasreddine et al., 2005) was used to assess cognitive status, and a MCI diagnosis was confirmed using standardized neuropsychological testing and a physician’s exam. MANOVA was calculated to compare young and older adults with and without MCI on oculomotor and vestibular function. Chi-square analysis was calculated to examine the proportion of clinically significant unilateral weakness among groups. Results indicated the young adult group showed shorter saccade latencies than either CNOA or MCI groups. The MCI group also showed both a higher mean unilateral caloric weakness and a higher occurrence of unilateral caloric weakness than either young adult or CNOA groups. The young adult group showed larger P1-N1 amplitudes than either CNOA or MCI groups for cervical VEMPs. There were no additional group differences on remaining oculomotor or vestibular measures. These results indicate older adults with MCI may show vestibular asymmetry assessed using bithermal caloric irrigation, however, these findings are not conclusive.
1. Introduction

Cognitive impairment, such as dementia, is often cited as the most feared condition that older adults face (Corner & Bond, 2004; Morris et al., 2001). MCI is conceptualized as a transitional state between normal cognitive function and dementia. It is defined as a clinical condition with significant impairment(s) in one or more cognitive domains, in the presence of otherwise normal global functioning, that is not severe enough to warrant a diagnosis of dementia (Petersen, 2004). The prevalence of MCI among older adults in the United States is reportedly between 18.8% and 28.3% (Ward et al., 2012). Persons with MCI are more likely to progress to dementia, and approximately 12% of persons with MCI convert to dementia per year, a six-fold increase compared to older adults without MCI (Petersen et al., 1999). As the number of older adults and cases of cognitive impairment increases, so does the need for enhancements in approaches to early detection of cognitive decline (Alzheimer’s Association, 2019).

Current approaches to detection of cognitive decline include neurological and cognitive screening tools and neuropsychological tests, such as the MoCA (Nasreddine et al., 2005). Blood analysis, family interviews, a physician’s exam, and in some cases, neuroimaging are also used commonly used to help detect cognitive decline, however, these services are often not considered until the signs and symptoms of cognitive decline have progressed and noticeably interfere with conducting daily activities (Alzheimer’s Association, 2019). It has been suggested that apparent signs and symptoms of cognitive decline may be preceded by declines in both sensory and motor systems by several years (Albers et al., 2015; Kluger et al., 1997). Thus far, studies have established relationships between cognitive decline and peripheral hearing (Bush et al., 2015; Edwards et al., 2017), central auditory processing (Edwards et al., 2017; Gates et al., 2008; Gates et al., 2011; Gates et al., 2002; Gates et al., 1995), and auditory event-related potentials (I.e.g.,
Balance is the result of multisensory processing and integration. The oculomotor system helps to maintain balance by generating eye movements to maintain stability of images during motion. The oculomotor system helps facilitate clear and stable vision while the head is in motion. There are two types of eye movements that work to: 1) ensure image stability on the retina during motion; and 2) direct the center of the field of vision, where visual acuity is highest, to objects of interest. Together these types of eye movements work to hold an image on the retina during static and dynamic head movement, bring an image quickly onto the fovea, hold slow moving objects on the fovea, and bring images into view for both eyes. The vestibular system senses motion of the head to and the sensory receptors transmit information to the central vestibular pathways to control reflexes and perceptions mediated by the vestibular system to maintain balance. The vestibular system is made up of five sensory organ receptors which transduce the angular velocity and linear acceleration of head movements. These receptor organs are matched on the opposite side of the head and include: three semicircular canals ([SCCs]; anterior, horizontal, posterior), which transduce angular velocity and two otolith organs (the utricle and saccule), which transduce linear acceleration in the horizontal and vertical planes, respectively (Balog & Honrubia, 2001; Blanks et al., 1985; Katz et al., 2009). Together the SCCs and otolith organs respond to static and dynamic changes in head position relative to gravity in three-dimensional space. Collectively, the sensory information from the afferent hair cell
receptors of the SCCs and otolith organs regarding head position and orientation in space is transmitted to the inferior and superior portions of the vestibular nerve (Angelaki & Dickman, 2019; Desmond, 2011; Previc, 2013; Vitte et al., 1996). Vestibular sensory information is further transmitted to the vestibular nuclear complex which integrate signals from both labyrinths and mediate three primary vestibular reflexes (Baloh & Honrubia, 1990). The vestibulo-ocular reflex (VOR) is a reflexive eye movement in response to head movement, commonly assessed to quantify generalized loss in vestibular sensitivity (Baloh et al., 2001; Richter, 1980). This reflex pathway generates voluntary and compensatory eye movements in order to maintain clear vision when the head is in motion (Leigh & Zee, 2015). The vestibulo-spinal reflex (VSR) is also an important reflex for stabilizing the head and maintaining upright stance by triggering muscle activity in the neck, trunk, and extremities (Highstein, 1996). The vestibulo-collic reflex (VCR) is involved in stabilizing head position in space during active motion of the body. Abnormal vestibular and oculomotor function can suggest abnormalities in vestibular reflexes, lead to sensations that reflect abnormal information about motion from the vestibular receptors, and may be signs of neurologic disease (Desmond, 2011; Jacobson & Shephard, 2014).

Balance function is evaluated using a variety of oculomotor and vestibular screening measures and clinical tests. Screening measures are brief informal screening measures for balance that are used to help identify abnormal oculomotor or vestibular function (Jacobson & Shephard, 2014), while clinical tests are used to objectively assess components of the oculomotor or vestibular systems to confirm a diagnosis (e.g., saccule, superior vestibular nerve, etc.). VNG refers to a group of clinical tests that provides information about oculomotor and vestibular abilities needed for maintaining visual contact within the environment and is helpful in assessment of the VOR. VNG tracks eye movement to assess oculomotor function by recording
eye movements using digital video image technology. Commonly assessed eye movements include: fast eye movement (saccades), slow eye movement (smooth pursuit), optokinetic responses, gaze, and simultaneous movement of both eyes (vergence). These oculomotor subtests are modulated by the cerebellum and abnormalities on these tests may be signs of neurologic disease (Desmond, 2011). The remaining VNG subtests are used to record changes in eye movement relative to changes in head and body position and vestibular asymmetry. Positional and positioning subtests are used to assess how the vestibular system responds to changes in head and body position, respectively. Caloric irrigations are used to assess the presence and symmetry of vestibular responsiveness by stimulating the horizontal SCC and simulating low-frequency head movements analogous to speeds of ~ 0.002 – 0.004 Hz. VEMPs are used to assess the otolith organs and vestibular portions of cranial nerve VIII (vestibulo-cochlear nerve). Cervical VEMPs (cVEMPs) assess the saccule and inferior portion of the vestibular nerve (Colebatch & Halmagyi, 1992) and are recorded from the ipsilateral sternocleidomastoid, while ocular VEMPs (oVEMPs) assess the utricle and superior portion of the vestibular nerve (Cuthoys, 2010; Iwasaki et al., 2009) and are recorded from the contralateral inferior oblique.

Age-related changes in sensory and motor function specific to the oculomotor and vestibular systems are known to occur with advancing age. For example, fast and slow eye movement linked to maintaining balance and stabilization are known to decrease with age (Abel et al., 1983; Kerber et al., 2006; Seferlis et al., 2015; Spooner et al., 1980; Warabi et al., 1984). Vestibular evoked-myogenic potentials are also known to decrease with age (Basta et al., 2007; Piker et al., 2015), as early as 40 years (Piker et al., 2015). Generally, VEMP responses in older adults are characterized by decreased amplitudes or absent responses (Janky & Shepard, 2009; Piker et al., 2015). Anatomical studies on the peripheral labyrinths have shown attrition of neural
and sensory cells as a function of age (Herdman et al., 2000; Johnsson, 1971; Katsarkas, 1994). The reduction in hair cells is generally symmetrical on both sides, whereas a vestibular pathology usually results in an asymmetry between the left and right labyrinths, or absent or in some cases a reduced vestibular function bilaterally.

The vestibulo-cortical connections disrupted in vestibular loss have been well-examined. Thus far, the vestibular system has shown to activate a broad cortical network including the insula, superior temporal gyrus, hippocampus, and inferior parietal lobule (Dieterich & Brandt, 2008; Hufner et al., 2009; Ventre-Dominey, 2014; Yardley et al., 2001). Studies have also reported on the relationship between vestibular function and various domains of cognition (e.g., attention, processing speed, visuospatial ability, etc.) showing links between vestibular impairment, working memory, spatial ability, executive function (Grimm et al., 1989; Risey & Briner, 1990), and attention (Redfern et al., 2004). Overall, studies are in support of a relationship between vestibular and cognitive status; however, the relationship between peripheral vestibular sensory function and cognitive decline in older adults remains less clear.

Thus far, studies have examined the relationship between oculomotor function and cognitive decline. Garbutt et al. (2008) and Boxer et al. (2006) compared oculomotor abnormalities associated with various neurologic disorders, including AD. Findings showed longer latencies for fast and slow eye movement in participants with AD compared to controls. Yang et al. (2013) compared horizontal and vertical saccades in amnestic MCI (aMCI) and AD groups. The AD and aMCI groups showed longer saccade latencies compared to controls. Oculomotor function has also been correlated with global cognition and brain volume. Yang et al. (2013) reported a correlation between saccade latency and cognitive status, measured using the Mini Mental State Examination (Folstein et al., 1975), in older adults with AD. Boxer et al.
also reported saccadic accuracy was correlated with brain volume and measures of
cognitive function. Other studies have shown strong relationships between oculomotor function
and measures of cognition (Crawford et al., 2005; Shafiq-Antonacci et al., 2003).

Studies report differences on clinical tests of otolith function in groups with and without
various degrees of cognitive decline. Harun et al. (2016) showed a higher occurrence of
bilaterally absent VEMPs and lower peak amplitudes in older adults with AD compared to
controls. Harun et al. (2016) reported no group differences between older adults with and without
MCI on VEMP peak amplitudes. Latency VEMP data were not reported for this study, however,
latency data was reported by Birdane et al. (2012). Birdane et al. (2012) reported longer mean
latencies for the p13 component of the cVEMP response in a combined group of AD and MCI
participants compared to controls, however, it is not possible to parse out the differences between
MCI and AD groups. While these studies are suggestive of abnormal balance function
characterized by abnormal oculomotor and vestibular function, this area of research would
benefit from more rigorous research with well-defined groups, and standardized
neuropsychological tests.

The purpose of this study was to examine oculomotor and vestibular function in young
adult, CNOA, and MCI groups. Oculomotor and vestibular function were assessed using VNG,
VEMPs, mCTSIB, and Fukuda Stepping test. We hypothesized the young adult group would
show better performance on all measures compared to either CNOA or MCI groups. For
oculomotor testing we hypothesized the MCI group would show reduced accuracy, longer
latencies, and slower peak velocities for saccadic subtests, reduced gain for smooth pursuit
tracking subtests, slow phase velocities outside of the normal range for optokinetic tracking,
positionals and positioning tests compared to the CNOA group. We further hypothesized the
MCI group would show caloric responses indicating clinically significant unilateral weakness compared to the CNOA group. Little is known about the impact of cognitive impairment on performance on measures that assess the VSR (i.e., Fukuda Stepping Test, etc.); therefore, these assessments were included for enhanced characterization of vestibular function among older adults with MCI. For VEMP, we hypothesized the MCI group responses would show smaller P1-N1 peak amplitudes and longer peak latencies compared to CNOA groups.

2. Method

2.1 Participants

Forty-four participants were recruited and screened for this study. Older adult participants (n = 27) age 60 and older were recruited from the Keys to Staying Sharp randomized clinical trial (RCT, NCT03528486). For the Keys to Staying Sharp study eligible participants had a MoCA score ≥ 20, binocular near visual acuity of 20/50 or better, pure-tone thresholds <70 dB HL in the mid-frequency range (e.g., 1000, 2000 Hz) in at least one ear, self-reported proficiency in the ability to speak, understand, and read English. Participants were excluded from the Keys to Staying Sharp study due to: Geriatric Depression Scale score ≥ 5; previous participation in intervention studies; completion of 10 or more hours of a computerized cognitive intervention programs (e.g., Lumosity, Brain HQ, Lace, CogMed, CogniFit); enrollment in a concurrent research study; unavailability for two or more weeks during the study period; plans to undergo chemotherapy or radiation treatment or other procedures requiring anesthesia during the study period; four or more years of formal music training; concurrent participation in any music activities; difficulty or pain moving hands or fingers, or neuropathy affecting hands; a TIA that occurred within the last 18 months; self-reported history of neurological disorder; or inability or unwillingness to give written informed consent. Following the neuropsychological evaluation,
participants who obtained a Clinical Dementia Rating Scale score ≥ 1 or a clinical diagnosis of dementia or other disorder. Only older adult participants eligible for the Keys to Staying Sharp study were recruited for the present study. Young adult participants were recruited from the Tampa Bay Area, including the Department of Communication Sciences and Disorders at the University of South Florida. Inclusion criteria for all participants for the present study included: willingness to be observed by clinical students for training purpose; willingness to have verbal responses audio recorded; no discomfort moving the head in the horizontal and vertical plane; no recent history of neck surgery or trauma that restricts torsional movement; and no known allergies to skin lotions, topical creams, or gel. Forty-two participants remained eligible for the present study: 15 young adult, 13 CNOA, and 14 older adults with MCI. One older adult participant was excluded from this study because they were previously deemed ineligible for the Keys to Staying Sharp randomized clinical trial due to availability to participate for the duration of the study.

2.2 Measures

2.2.1 Hearing Function

All audiometric equipment was calibrated, properly functioning, and located in an environment free of electrical interference as specified in American National Standards Institute (ANSI) Standard s3.6 – 2010 (American National Standards Institute, 2010). Air conduction hearing thresholds were assessed at 500, 1000, 2000, 4000, 6000 and 8000 Hz using ER-30 insert earphones. Bone conduction thresholds were also assessed at 500 Hz. It is established that the VEMP response to air-conducted stimuli present in individuals with normal vestibular function even in the presence of profound sensorineural hearing loss; however, a conductive hearing loss will attenuate the stimulus transmitted to the otolith organs resulting in reduced or
absent VEMP responses (Colebatch & Halmagyi, 1992; Jacobson & Shephard, 2014). Middle ear pathologies are also known to confound the results of caloric stimulation due to alteration of thermal conductivity across the middle ear space. To ensure there were no temperature transfer effects on caloric irrigations related to middle ear pathology or negative effects of conductive hearing loss on VEMP responses, otoscopy and tympanometry were completed to confirm unobstructed auditory canals and adequate middle ear function. Participants who presented with unilateral or bilateral air-bone gaps (ABGs) > 10 dB at 500 Hz did not complete VEMP testing for the affected ear(s) but remained eligible for the study. A total of five participants presented with unilateral ABGs for the right (2) and left (3) ears. Bone conduction responses were not obtained for one participant, therefore the ABG could not be calculated and VEMPs were not completed.

2.2.2 Cognitive Function

The MoCA has 94% sensitivity to identify dementia and 90% sensitivity to identify MCI (Nasreddine et al., 2005). Qualified psychometricians and clinicians administered these tests and followed the Alzheimer’s Association/National Institute on Aging guidelines for the diagnosis or exclusion of MCI (Albert et al., 2011). The neuropsychological evaluation included subtests of the National Alzheimer’s Coordinating Center Uniform Data Set (NACC) neuropsychological battery (Morris et al., 2006). The NACC battery consists of multiple subtests which include the Clinical Dementia Rating (CDR) scale (Morris, 1997), the Multilingual Naming Test (MINT; Gollan et al., 2012), the Benson Complex Figure Copy immediate and delayed subtests (Possin et al., 2011), the Craft Story 21 immediate and delayed recall subtests (Craft et al., 1996), the Functional Assessment Scale (FAS; Pfeffer et al., 1982). The Clinical Diagnosis Form was completed by a study physician who specialized in geriatric psychiatry.
2.2.3 Balance Function

Oculomotor and vestibular contributions to balance were assessed in the present study. Oculomotor and vestibular function were assessed using VNG (Glackin & Proctor, 1984; Proctor et al., 1981). Oculomotor subtests of VNG (e.g., gaze, saccades, smooth pursuit, optokinetic tracking) were used to assess fast and slow eye movements. Positioning and positionals subtests assessed eye movements related to changes in head and body position. Caloric irrigations assessed the horizontal SCCs, VOR, and the vestibulo-cochlear nerve. VEMPs (Colebatch & Halmagyi, 1992; Colebatch et al., 1994), mCTSIB, and the Fukuda Stepping test (Fukuda, 1959; Shumway-Cook & Horak, 1986; Wrisley & Whitney, 2004) assessed the VSR, otolith organs, and both branches of the vestibulo-cochlear nerve.

2.2.3.1 Videonystagmography

VNG is commonly used to assess peripheral vestibular function (Bhansali & Honrubia, 1999; Desmond, 2011). VNG refers to a battery of tests that assess eye movements to help evaluate vestibular function. The battery consists of three components: oculomotor testing, positioning and positional testing, and caloric testing. The oculomotor subtests assess ability to track a moving target using eyes only; positioning and positional subtests assess the effect of dynamic and static changes in head and body position on the vestibular system; caloric testing is used to assess the presence and asymmetry of vestibular responsiveness by stimulating the horizontal SCC and simulating low-frequency head movement. The VNG offers: 1) examination of oculomotor system impairment; 2) examination of one labyrinth independent of the other and localization of the side of lesion; and 3) the ability to quantify and document nystagmus for analysis and clinical interpretation (Desmond, 2011). The present study used the ICS Chartr 200 VNG system to administer the VNG.
2.2.3.1 Oculomotor Testing

There are different types of eye movements that work to bring the image of interest to the foveae for both eyes, and to maintain image stability on the retina while the head undergoes static and dynamic motion (Jacobson & Shephard, 2014). The oculomotor subtests used in the VNG battery included gaze stability, saccadic testing, smooth pursuit tracking, and optokinetic nystagmus. The gaze stability subtest assessed the ability to maintain gaze fixed on a target while keeping the head oriented at 0° azimuth with the eyes positioned 30° to the left and right. Saccades are rapid eye movements made to bring an object of interest into the center of the line of sight, on the fovea. The saccades subtest was used to assess the ability to move eyes rapidly from one target to another. Smooth pursuit eye movements help to maintain gaze on slowly moving objects within the visual field. The smooth pursuit (tracking) subtest was used to assess the ability to track a smoothly moving target that varied in frequency within the visual field. Optokinetic (OKN) tracking eye movements are generated by movement of a large visual scene and help to stabilize images on the retina during sustained head rotation (Jacobson & Shephard, 2014). The OKN tracking subtest was used to assess nystagmus generated by tracking repeated moving objects across the visual field.

2.2.3.1.2 Positioning and Positional Tests

The Dix-Hallpike maneuver (Dix & Hallpike, 1952), a positioning subtest, was used to evaluate changes in eye movement during active head and body movements. Specifically, this test is the gold standard for identification of benign paroxysmal positional vertigo (BPPV). Positional tests were used to assess whether the vestibular system responds normally and symmetrically to changes in head position.
2.2.3.1.3 Caloric Irrigation

Caloric irrigation was used to assess horizontal SCC response symmetry for low-frequency equivalent stimulation. Specifically, bithermal (warm, cool) air irrigations assessed the horizontal SCC and superior vestibular nerve function on each side. The temperature of the air stimulus was set to 50° and 26° Celsius for the warm and cool irrigations, respectively. Warm irrigations (right, left) were completed first followed by cool irrigations (right, left). Caloric irrigations were also completed using the ICS Chartr 200 VNG system (GN Otometrics, 2015). Irrigations were performed for ~60 seconds per ear and temperature using the Otometrics NCA200 irrigator.

2.2.3.2 Vestibular Evoked Myogenic Potentials

Known sources of variability in recording oVEMP responses include patient head position and electrode placement. Sandhu et al. (2013) examined the effect of electrode position on amplitude and latency for oVEMP responses. Findings showed the location of recording electrodes altered response amplitude, and that positioning the reference electrode over the tendon of the inferior oblique muscle reduces the likelihood of reference contamination yielding a larger amplitude response: this is known as the belly-tendon montage. The belly-tendon montage positions the active (non-inverting) electrode lateral to the midline of the lower margin of the contralateral eyelid, with the reference (inverting) electrode positioned on the inner canthus of the contralateral eye. It is further suggested that placing participants in the supine position prior to a sudden high-intensity auditory stimulus reduces the maximum obtainable response by preloading the utricular maculae in the tilt position (Shojaku et al., 2008; Taylor et al., 2014; Wang et al., 2014). For this reason, the sitting position is recommended to lessen the baseline stimulation of the utricular maculae. Recently, Makowiec et al. (2017) examined
optimal recording parameters for evoking oVEMP responses, and demonstrated the belly-tendon montage recorded with participants in the sitting position yielded larger amplitudes and shorter latencies compared to other recording parameters. Similar to oVEMPs, cVEMPs are influenced by variations in stimulus and recording parameters and optimal parameters are suggested by various studies (Wuyts et al., 2007; Young, 2006; Zapala, 2007; Zhou & Cox, 2004). Variability of the cVEMP response can depend on sternocleidomastoid (SCM) activation method, electrode montage, transducer type, amplifier gain, filter settings, time window for recording, number of sweeps, and tone burst frequency (Murofushi, 2001a, 2001b; Welgampola, M. S. & Colebatch, 2005; Zhou & Cox, 2004). Meyer et al. (2015) report air-conduction stimuli presented at 95 dB nHL with ~ 5 Hz stimulation rate, one millisecond (ms) rise and fall times coupled with a two ms plateau are considered optimal parameters for eliciting a cVEMP response using a tone-burst stimulus. In line with common practice, the present study recorded the cVEMP response with the active electrode positioned on the upper half and middle third of the SCM, and the reference electrode was positioned along the lateral portion of the upper sternum (Colebatch & Halmagyi, 1992; Meyer et al., 2015).

2.2.3.3 Vestibulo-Spinal Reflex Screening Tools

The mCTSIB (Wrisley & Whitney, 2004) was used to assess the ability to make use of sensory inputs when one or more sensory systems become unreliable. The mCTSIB is a multi-surface screening that consists of four conditions: 1) eyes open, firm surface; 2) eyes closed firm surface; 3) eyes open, foam surface; and 4) eyes closed, foam surface. The first condition made use of all available sensory system information (e.g., vision, somatosensory, and vestibular) for maintaining static balance and postural control. The second condition restricted participants to rely only on somatosensory and vestibular inputs for maintaining balance and postural control.
For the third condition use of the specialized foam surface made the somatosensory feedback from the lower limbs unreliable and increased reliance on visual and vestibular inputs for maintaining balance and postural control. The fourth condition removed visual and somatosensory inputs, restricting reliance on vestibular inputs alone for maintaining balance. The mCTSIB has a reported test-retest reliability of $r = 0.75$ in older (Anacker & Di Fabio, 1992), and an $r = 0.99$ for test-retest and inter-rater reliability (Cohen et al., 1993). The mCTSIB has a reported sensitivity of 88% in both the eyes open and closed conditions (Wrisley & Whitney, 2004), and reported specificity rates of 44% in the eyes open condition, and 50% in the eyes closed condition (Wrisley & Whitney, 2004). Condition four of the mCTSIB (standing on foam surface with eyes closed) has a reported sensitivity of 83% and specificity of 36% with feet apart (Wrisley & Whitney, 2004).

The Fukuda Stepping test was used to identify peripheral vestibular system impairment manifested as an asymmetry in lower extremity vestibulo-spinal reflex “tone” (Fukuda, 1959; Jacobson & Shephard, 2014). A rotation ≥ 45° from the start position was considered suggestive of peripheral vestibular impairment. Studies report moderate reliability angle rotation (Intra-class correlation coefficient = .66), angle of displacement (Intra-class correlation coefficient = .66), and distance displacement (Intra-class correlation coefficient = .69) for the 50-step Fukuda Stepping test (Bonanni & Newton, 1998). The Fukuda Stepping test also has reported sensitivity ranging from ~60 – 71% and ~60% specificity (Honaker et al., 2009; McCaslin et al., 2008; Moffat et al., 1989).
2.3 Procedure

2.3.1 Cognitive Function

The purpose of the neuropsychological evaluation was to confirm a diagnosis of MCI. All participants were administered the MoCA to detect cognitive decline. Older adults who scored ≥ 26 were considered cognitively normal older adults (CNOA) and those who scored ≤ 20 on the MoCA were excluded (Nasreddine et al., 2005). Those older adults who obtained a MoCA score of 25 or less completed standardized neuropsychological tests and a physician’s exam. In order to rule out medical causes of cognitive decline that are treatable, participants who scored 20-25 on the MoCA also provided lab results (e.g., complete blood count, B12, Vitamin D, folic acid, etc.) from the past year. Lab results were provided by the participant or completed on site at the request of the physician. Any results not within normal limits were reviewed by the study physician. Those without any clinically significant abnormalities continued in the study. Testers were not blinded to participant cognitive status.

2.3.2 Oculomotor Testing

All oculomotor testing was completed using the standard Otometrics lightbar. All testing was performed in a dimly lit testing room to ensure proper visualization of participants’ eyes and the target. Calibration procedures were completed at the start of the battery to quantify eccentric eye movements, and default calibration options were available for use when individual calibrations could not be obtained (Norman & Brown, 1999). Default calibrations were used for one CNOA and two MCI participants. Oculomotor subtests were completed in the seated position approximately 3.8 – 4.4 feet from the light bar. VNG hardware included a range sensor to continuously sample the distance between the participant and the light bar during testing to ensure reliable results. The distance was updated every three seconds and displayed during the
test. Testers were prompted to make adjustments if the participant moved outside of the acceptable range. If a subtest was administered with the participant outside of the acceptable range for more than 10% of the test, a message was displayed at the conclusion of the test, announcing the out-of-range status (GN Otometrics, 2015), prompting for repeat testing.

For gaze, participants were instructed to stare at the target to the right or left of the light bar using their eyes only while keeping the head still. This position was maintained for approximately 10 – 15 seconds for each side (right, left). This subtest is often used to identify spontaneous and gaze-evoked nystagmus during steady fixation. Remarkable findings on this subtest can reflect abnormalities in peripheral or vestibular and ocular motor systems (Desmond, 2011; Jacobson & Shephard, 2014). Gaze evoked and spontaneous nystagmus are often reported using a combination of using quantitative and descriptive techniques. Nystagmus is clinically characterized by direction, presence or absence of fixation, and changes in velocity of the fast and slow components of eye movement. Specific characteristics suggestive of nystagmus of peripheral origin include enhancement of nystagmus in the same direction with fixation removed, and direction-fixed nystagmus that increases in intensity as gaze increases in the direction of the fast component. Spontaneous nystagmus is may also be present in healthy individuals (Levo et al., 2004). Key findings suggestive of a central pathology include direction changing nystagmus based on gaze direction, or purely vertical or torsional nystagmus. Nystagmus is often considered clinically significant when the slow component of the eye movement ≥ six degrees per second (GN Otometrics, 2015; Handelsman & Shephard, 2008; Linstrom, 1992; Shepard & Telian, 1996).

The present study used the ICS Chartr 200 analysis software to quantify the strength of nystagmus. A 140-second section of the tracing is identified and, for each second, the slow phase
velocity of the individual beats of nystagmus are measured. To calculate the peak slow phase velocity the software identifies left and right slow phase velocities in a specific time window (e.g., 140 – second). Velocities were calculated for left and right movements, sorted from highest to lowest, and three fastest velocities are averaged. The average velocity is further compared to the most extreme data point (- or +), with the faster value reported as the peak velocity (GN Otometrics, 2015). The present study recorded peak slow phase velocity (SPV) for right and left gaze.

For saccades, visual stimuli were generated pseudo-randomly and presented along the light bar of the ICS Charrt 200 VNG system. Targets appeared along the light bar within a range of 5 – 30° from center for ~1 – 4 seconds. Participants were instructed to follow the target as it moved randomly along the light bar using their eyes only keeping the head still. Performance was recorded as the accuracy, latency, and peak velocity for leftward and rightward eye movements. Eye movements that occurred too early (250 ms before – 75 ms after target movement), too late (600 + ms after target movement), or in the wrong direction were identified as artifact and rejected by the ICS VNG software. Saccadic velocity was measured as the peak speed of eye movement when adjusting gaze from one visual stimulus to another (Jacobson, 1993). Responses are considered clinically abnormal if slower than 430° per second for large-amplitude (30°) saccades and slower than ~ 200° per second for small-amplitude (10 – 15°) saccades Desmond (2011). Peak latency is often considered clinically abnormal at ~260 ms or longer (Desmond, 2011). Saccadic testing approximated 40 seconds in duration and did not exceed five minutes.

For smooth pursuit, the visual target oscillated 15 – 20° from the center of the light bar with a default amplitude of 16.7°. The visual stimulus moved in a sinusoidal pattern of three
cycles for each of the following frequencies: 0.2, 0.3, 0.4, 0.5, 0.6, 0.7 Hz. This procedure was repeated until the subtest was terminated by the tester, or the test exceeded three minutes. Participants were instructed to follow the target along the light bar using their eyes only and keeping the head still. Performance was recorded as gain, the ratio of eye velocity to visual stimulus velocity, for leftward and rightward eye movements. For gain, the velocity of the visual stimulus was compared to eye movements across the same period. Saccades defined as movements of more than 15° per second faster than the stimulus were eliminated by the ICS software.

For OKN tracking, stimuli consisted of a series of light targets that moved continuously along the light bar at 20° per second. Participants were instructed to count the targets as they passed through the center of the light bar using their eyes only and keeping the head still. The peak velocity was obtained for both leftward and rightward eye movements. To calculate velocity gain, the peak eye velocity was identified and divided by the target velocity. Gain was calculated for left and rightward target movement. Gains for both eyes are expected to within 25% of each other. This subtest accounted for ~30 seconds of testing.

2.3.3 Positioning and Positionals

Test began with participants in an upright seated position at the edge of the examiner’s table. Testing was completed with vision denied (lid of goggles closed). Prior to closing the lid for the goggles, participants were instructed to keep the eyes open with the head turned ~45° to the right (and left). This position was maintained for ~20 seconds after which the tester carefully reclined the participant into the supine position with head-hanging while maintaining the head at ~45° to the right (and left). The modified Dix-Hallpike was used by placing a pillow behind the participant to alleviate pressure on the lower back and ensure comfort during testing for all
participants (ref). Participants maintained this position for approximately ~30 seconds (or until evoked nystagmus ceased). Testers then helped participants transition back to the seated upright position while keeping the head turned ~45° to the right (and left). Participants maintained this position for ~30 seconds before relaxing into the neutral position at 0° azimuth. The procedure was repeated for the opposite side. The SPV for eye movements were recorded for the right and left side. For positionals, eye movements were recorded with vision denied. Participants were instructed to keep the eyes open while looking forward in the neutral position. With the support of the tester, participants rotated the head ~ 90° to the right (and left). This position was maintained for ~20 seconds. The tester then guided the participant back to the neutral position and the procedure was performed for the opposite side. Peak velocity was recorded for the right and left sides.

2.3.4 Caloric Irrigations

Participants were elevated ~30° to position the horizontal semicircular canal in the vertical plane for maximum stimulation (Fitzgerald & Hallpike, 1942), and the ear canals were irrigated for ~60 seconds for each temperature on each side. Following irrigation, the participant was engaged in a mental alerting task (e.g., listing girls’ name that begin with the letter “A”, etc.) to distract from suppressing any evoked nystagmus. Participants were also instructed to focus on a fixation light presented within the goggles while the nystagmus was observed for suppression. This procedure was repeated for the opposite side. For the caloric tests, the peak responses were identified and saved for use in the system’s calculation of caloric (unilateral) weakness. Caloric asymmetry was calculated using all four caloric irrigations and a unilateral caloric weakness ≥ 25% was considered clinically significant. Caloric weakness was calculated using the formula:
Unilateral Weakness = \frac{(\text{Right Cool} - \text{Right Warm}) - (\text{Left Warm} - \text{Left Cool})}{(\text{Right Cool} - \text{Right Warm}) + (\text{Left Warm} - \text{Left Cool})} \times 100

The caloric asymmetry was obtained using ICS Chrtr 200 software and the mean caloric asymmetry was calculated for each group for comparison in MANOVA.

2.3.5 Vestibular Evoked Myogenic Potentials

VEMPs were elicited using 500 and 750 Hz tone burst stimuli which were presented via ER3 – 14A insert earphones at 95 dB nHL. A minimum of two recordings were completed for each ear for each stimulus type (500 Hz, 750 Hz). Instances in which the minimum number of VEMP recordings were not obtained are detailed in Table 2. The N1-P1 amplitude and peak latencies were recorded. Skin surface electrodes were applied to participants’ sternum, neck and head areas. Electrode sites were prepared and cleaned in order to obtain acceptably low skin impedances of 5 kΩ or lower (Colebatch & Halmagyi, 1992). For those participants with ABGs > 10 dB VEMP testing was not completed for the affected ear. Five participants presented with ABGs > 10 dB and VEMPs were not obtained for the right ear for three participants and the left ear for two participants.

The oVEMP response was recorded from sites beneath the ipsilateral and contralateral eyes following monaural stimulation. The active electrode was positioned lateral to the midline of the lower margin of the contralateral eyelid. The reference electrode was positioned on the inner canthus of the contralateral eye over the tendon of the inferior oblique muscle. The oVEMP rise/fall times consisted of one cycle and plateau time of two cycles, with a stimulation rate of 5.2 Hz. Participants were instructed to focus on a visual target with gaze elevated 30° above midline gaze, and to maintain an upward gaze for approximately 30 seconds. A visual target was placed on the ceiling at +30 degrees with reference to the midline when participants were in the upright sitting position. The cVEMP rise/fall times consisted of one cycle and plateau time of
two cycles, with a stimulation rate of 5 Hz. Participants were instructed to lift, turn and hold their head, from the supine position for a duration of 30 seconds. To control variability related to differences in SCM contraction participants were to instructed to generate a pressure of ~ 40 millimeters of mercury (mmHg) measured using a blood pressure cuff positioned between the participant’s head and neck during the head turn (Vanspauwen et al., 2006). Interaural amplitude asymmetry ratios (IARs) were calculated using the formula:

\[ \text{IAR} = \frac{\text{Amplitude right VEMP} - \text{Amplitude left VEMP}}{\text{Amplitude left VEMP} + \text{Amplitude right VEMP}} \times 100, \]

2.3.6 Vestibulo-Spinal Reflex Screening Tools

All vestibular and oculomotor function testing was completed by two audiologists and one first year audiology student. Study testers demonstrated intermediate to advanced levels of experience and proficiency in administering these tests. All vestibular and oculomotor testing took place in the vestibular testing room at the University of South Florida Hearing Clinic. For the mCTSIB, the Balance Performance Foam issued by the American Institute of Balance, which has been standardized in patients from 3 – 79 years of age with a maximum weight of 350 pounds (159 kilograms), was used to administer the mCTSIB. The dimensions of the foam were 24 x 12 x 6 inches which allowed testing for taller patients with a widened base of support (American Institute of Balance). Participants completed testing on the firm surface with eyes open and closed, followed by the specialized foam surface with eyes open and closed. All testing was completed in the standing position with the participant facing the testing room door, feet shoulder width apart, and arms positioned across the chest with the palms of the hands touching the opposite shoulders. Participants completed each condition up to three times for a duration of 30 seconds timed using a stopwatch. Time was stopped and recorded if the participant: 1) deviated from the crossed arm position; 2) opened their eyes in an eyes closed condition; 3)
repositioned the feet; or 4) required manual assistance from the study tester. A trial was successfully completed if the participant was able to maintain the standing position unassisted for 30 seconds. A maximum of three trials were performed for each condition. Trials were performed until the participant successfully maintained the standing position for 30 seconds or completed three 30-second trials to the best of their ability. Performance was recorded as the total score across the four conditions. Testers administered this test in approximately 10 minutes.

The Fukuda Stepping test was completed with eyes open and eyes closed. A reference marker map was designed and implemented to measure displacement and angle deviation from the initial to the final position. Participants were oriented to the start position marked by a 12 x 3-inch green marker positioned in the horizontal plane. Feet were positioned shoulder width apart with arms extended (straight out) in front of the body. Participants were instructed to march at their own pace for 50 steps, and on the 50th step they were instructed to stop and to briefly remain in the final position. The angle, direction, and displacement (in inches) from the start to the final position were recorded. This procedure was completed for two trials of each condition (eyes open, eyes closed). An average displacement score was calculated for each condition for data analysis. Testers administered two trials of each condition in approximately 10 minutes.

2.4 Data Analysis

Demographic details were examined for each group. Means (M) and standard deviations (SDs) of oculomotor and vestibular measures were calculated across groups. Several analyses were calculated to: 1) examine relationships between measures of oculomotor and vestibular function; 2) compare oculomotor and vestibular function in young adult, CNOA, and MCI groups; and 3) compare the proportion of clinical oculomotor or vestibular abnormality among groups (see Table 1). Oculomotor or vestibular subtests that showed moderate to strong
associations with a Pearson $r \geq .3$ were combined into a composite. Alpha values were set to .05. Effect sizes were reported as partial eta squared ($\eta^2_p$).

**Table 1 Oculomotor and Vestibular Function Analyses**

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson correlation</td>
<td>To examine relationships between measures of oculomotor and vestibular function.</td>
</tr>
<tr>
<td>MANOVA</td>
<td>To compare oculomotor and vestibular function in young adult, CNOA and MCI groups.</td>
</tr>
<tr>
<td>Chi-square</td>
<td>To compare the frequency of clinical oculomotor or vestibular abnormality.</td>
</tr>
</tbody>
</table>

*Note. MANOVA = multivariate analysis of variance.*

**3. Results**

Group demographics are presented in Table 1. MANOVA was calculated to examine group differences on hearing and education. A significant effect was found, Wilks’ Lambda = .692, $F = (6,74) = 4.49, p = .030, \eta^2_p = .168$. Fisher’s Least significant difference (LSD) post-hoc analyses showed hearing pure tone averages for the right $F(2, 39) = 6.49, p = .004, \eta^2_p = .25$, and left ear, $F(2, 39) = 4.84, p = .013, \eta^2_p = .20$, were significantly lower for the young adult group compared to either CNOA or MCI groups, $ps < .015$. There was no significant difference between CNOA or MCI groups on hearing pure-tone averages for the right or left ear, $ps > .869$. Similarly, there were no differences between CNOA and MCI groups on age, $p = .752$. There were no significant differences between groups on education, $F(2, 39) = .027, p = .973, \eta^2_p = .001$. Chi-Square analyses indicated no significant difference between groups for sex, $X^2 = 8.06, p = .018$, or race, $X^2 = 9.22, p = .512$. 
Table 2 Participant Demographics

<table>
<thead>
<tr>
<th>Group</th>
<th>MoCA M(SD)</th>
<th>Age M(SD)</th>
<th>% Female</th>
<th>% White</th>
<th>Education M(SD)</th>
<th>Left ear M(SD)</th>
<th>Right ear M(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YA (n = 15)</td>
<td>29.1 (.961)</td>
<td>26.6 (5.43)</td>
<td>86.7</td>
<td>53.3</td>
<td>16.5 (1.51)</td>
<td>8.2* (6.60)</td>
<td>9.2* (5.73)</td>
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<td>CNOA (n = 13)</td>
<td>25.7 (2.29)</td>
<td>72.9 (7.38)</td>
<td>53.8</td>
<td>76.9</td>
<td>16.6 (2.73)</td>
<td>27.8 (30.55)</td>
<td>23.6 (18.39)</td>
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<tr>
<td>MCI (n = 14)</td>
<td>23.9 (1.79)</td>
<td>73.7 (6.94)</td>
<td>35.7</td>
<td>78.6</td>
<td>16.6 (2.24)</td>
<td>29.05 (17.78)</td>
<td>24.4 (11.87)</td>
</tr>
</tbody>
</table>

Note.

MoCA = Montreal Cognitive Assessment; PTA = Pure Tone Average.

*p ≤ .05

3.1 Oculomotor and Vestibular Function

Pearson correlations were calculated among measures of oculomotor and vestibular function. Several moderate to strong correlations were found and are reported in Tables 3 – 3.3. Oculomotor measures performed for the right and left sides with correlations of .3 or greater were computed into five composite variables: gaze, smooth pursuit, saccades accuracy, saccades latency, and saccades peak velocity. For vestibular measures with multiple conditions such as, P1-N1 peak amplitudes, P1 latencies, N1 latencies (500 ,750 Hz) and Fukuda Stepping test performance (open, closed) were also computed into composites. MANOVA was calculated to compare oculomotor and vestibular function in young adult, CNOA and MCI groups. No significant effect was found, Wilks’ Lambda = .086, F = (44,18) = .983, p = .539, η²p = .71; however the purpose of this study was to compare oculomotor and vestibular sensory function in young adults and older adults with and without MCI, therefore, follow-up univariate analyses were calculated and are reported below.
Table 3 Correlations for Oculomotor Measures

<table>
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</table>

Note. 1 = left; 2 = right; OKN = optokinetic tracking; DH = Dix-Hallpike.

*p ≤ .05

**p ≤ .01
Table 3.2 Correlations for Vestibulo-Spinal Reflex Screening Tools

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<td>3. Fukuda – closed</td>
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* *p ≤ .01
Table 3.3 Correlations for Vestibular Measures

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<td>16. N1 latency</td>
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Note. a = 500 Hz stimulus; b = 750 Hz stimulus.

*p ≤ .05

**p ≤ .01
3.1.1 Videonystagmography

For VNG, there were significant differences between groups on saccade latency, $F(2, 30) = 6.59$, $p = .004$, $\eta^2_p = .31$, and unilateral caloric weakness, $F(2, 30) = 4.40$, $p = .0216$, $\eta^2_p = .23$. LSD post-hoc analyses showed shorter saccade latencies for young adult compared to either CNOA or MCI groups, $ps < .005$. There was no significant group difference on saccade latencies between CNOA and MCI groups, $p = .829$. For caloric irrigation, LSD post-hoc analyses showed a significant difference on unilateral caloric weakness between CNOA and MCI groups, $p = .047$, and between YA and MCI groups, $p = .007$. The MCI group showed a greater mean caloric weakness compared to either YA or CNOA groups. In contrast, there was no significant difference between young adult and CNOA groups on mean caloric weakness, $p = .575$. There were no additional group differences on saccadic peak velocity $F(2, 30) = .437$, $p = .650$, $\eta^2_p = .028$, accuracy, $F(2, 30) = .022$, $p = .978$, $\eta^2_p = .001$, OKN asymmetry, $F(2, 30) = 1.16$, $p = .326$, $\eta^2_p = .07$, smooth pursuit gain, $F(2, 30) = 1.24$, $p = .305$, $\eta^2_p = .08$, positionals for the left, $F(2, 30) = .411$, $p = .667$, $\eta^2_p = .03$, or right, $F(2, 30) = .006$, $p = .994$, $\eta^2_p = .00003$, positioning for the left, $F(2, 30) = .086$, $p = .917$, $\eta^2_p = .01$, positioning for the right, $F(2, 30) = 1.07$, $p = .357$, $\eta^2_p = .07$, or directional preponderance, $F(2, 30) = .484$, $p = .621$, $\eta^2_p = .03$. Additionally, chi-square analysis was calculated to compare the proportion of caloric unilateral weakness in YA, CNOA, and MCI groups. A significant interaction was found, $X^2 = 7.84$, $p = .020$. The MCI group was more likely to have a caloric unilateral weakness (69%) compared to either YA or CNOA groups.
Table 3.4 Oculomotor Group Performance

<table>
<thead>
<tr>
<th>Group</th>
<th>Gaze Gain M(SD)</th>
<th>Smooth Pursuit Gain M(SD)</th>
<th>Accuracy Latency M(SD)</th>
<th>Saccades Gain Peak Velocity M(SD)</th>
<th>OKN Gain M(SD)</th>
<th>Positionals SPV L M(SD) R M(SD)</th>
<th>Dix-Hallpike SPV L M(SD) R M(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YA</td>
<td>.00 (.00)</td>
<td>.75 (10.66)</td>
<td>88.57 (24.76)</td>
<td>168.07* (66.89)</td>
<td>0.15 (0.23)</td>
<td>0.20 (-0.13)</td>
<td>0.20 (-1.07)</td>
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<tr>
<td>(n = 15)</td>
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<tr>
<td>CNOA</td>
<td>.04 (-0.03)</td>
<td>89.00 (30.13)</td>
<td>211.31 (59.54)</td>
<td>417.19 (0.32)</td>
<td>0.08 (1.60)</td>
<td>1.25 (-0.08)</td>
<td>0.08 (-1.31)</td>
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<td>(n = 13)</td>
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<tr>
<td>MCI</td>
<td>-.04 (-1.12)</td>
<td>88.54 (18.86)</td>
<td>180.64 (82.36)</td>
<td>398.14 (179.62)</td>
<td>0.02 (0.18)</td>
<td>0.38 (-0.23)</td>
<td>0.92 (0.46)</td>
</tr>
<tr>
<td>(n = 13)</td>
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</table>

Note. YA = young adult; CNOA = cognitively normal older adult; MCI = Mild Cognitive Impairment; SP = smooth pursuit; OKN = optokinetic tracking asymmetry; SPV = slow phase velocity.

*p ≤ .05

Table 3.5 VNG Caloric Irrigations

<table>
<thead>
<tr>
<th>Group</th>
<th>Total Left SPV M(SD)</th>
<th>Total Right SPV M(SD)</th>
<th>UW % M(SD)</th>
<th>DP % M(SD)</th>
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<tr>
<td>YA</td>
<td>29.31 (15.68)</td>
<td>29.29 (11.44)</td>
<td>15.92 (8.32)</td>
<td>14.31 (18.57)</td>
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<td>(n = 13)</td>
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<tr>
<td>CNOA</td>
<td>27.31 (12.32)</td>
<td>36.62 (20.33)</td>
<td>23.15 (23.82)</td>
<td>25.77 (20.16)</td>
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<td>(n = 13)</td>
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</tr>
<tr>
<td>MCI</td>
<td>29.54 (20.42)</td>
<td>29.31 (18.98)</td>
<td>37.15* (25.49)</td>
<td>19.42 (12.21)</td>
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<td>(n = 14)</td>
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</table>

Note. YA = young adult; CNOA = cognitively normal older adult; MCI = Mild Cognitive Impairment; SPV = slow phase velocity; UW = unilateral weakness; DP = directional preponderance.

*p ≤ .05

3.1.2 Vestibular Evoked Myogenic Potentials

For oVEMPs, there were no significant differences between groups on P1-N1 amplitudes, $F(2, 30) = .092, p = .912, \eta^2 = .006$, P1 peak latency, $F(2, 30) = .445, p = .645, \eta^2 = .03$, N1 peak latency, $F(2, 30) = .809, p = .455, \eta^2 = .05$, or amplitude asymmetry, $F(2, 30) = 1.59, p = .220, \eta^2 = .10$, (see Table 3.1.1 – 3.1.2 for descriptive statistics).
For cVEMP s there was a significant group difference on P1-N1 peak amplitude, $F(2, 30) = 5.09, p = .012, \eta^2_p = .25$. LSD post-hoc analyses showed larger P1-N1 peak amplitudes for the YA group compared to either CNOA or MCI groups, $ps < .008$. There were no group differences on cVEMP amplitudes between CNOA or MCI groups, $p = .879$. There were no significant differences between groups on P1 peak latency, $F(2, 30) = 1.08, p = .352, \eta^2_p = .07$, N1 peak latency for 500 Hz, $F(2, 30) = 1.24, p = .303, \eta^2_p = .08$, N1 peak latency for 750 Hz, $F(2, 30) = 1.04, p = .367, \eta^2_p = .065$, or amplitude asymmetry, $F(2, 30) = 1.03, p = .369, \eta^2_p = .06$, (see Table 3.3.1 – 3.3.2 for cVEMP descriptive statistics).

### Table 3.6 Single Vestibular Evoked Myogenic Potential Recordings

<table>
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<tr>
<th>Group</th>
<th>oVEMP 500 Hz</th>
<th>oVEMP 750 Hz</th>
<th>cVEMP 500 Hz</th>
<th>cVEMP 750 Hz</th>
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<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>YA (n = 15)</td>
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<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CNOA (n = 13)</td>
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<td>0</td>
<td>4</td>
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<td>MCI (n = 14)</td>
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<td>3</td>
<td>0</td>
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</table>

Note. oVEMP = ocular vestibular evoked myogenic potential; cVEMP = cervical evoked myogenic potential; YA = young adult; CNOA = cognitively normal older adult; MCI = Mild Cognitive Impairment; Hz = Hertz.
Table 3.7 Vestibular Evoked Myogenic Group Performance

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<tr>
<td></td>
<td>Amplitude</td>
<td>Latency</td>
</tr>
<tr>
<td></td>
<td>P1-N1 M(SD)</td>
<td>Asymmetry M(SD)</td>
</tr>
<tr>
<td>YA</td>
<td>2.08 (.95)</td>
<td>20.47 (47.36)</td>
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<tr>
<td>(n = 15)</td>
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<tr>
<td>CNOA</td>
<td>2.76 (2.49)</td>
<td>-.42 (19.74)</td>
</tr>
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<tr>
<td>MCI</td>
<td>2.35 (1.07)</td>
<td>-.19 (26.03)</td>
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<tr>
<td>(n = 13)</td>
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</table>

Note. oVEMP = ocular vestibular evoked myogenic potential; cVEMP = cervical vestibular evoked myogenic potential

*p ≤ .05.

3.1.3 Vestibulo-Spinal Reflex Screening Tools

For the vestibulo-spinal reflex screening tools, there were no significant differences between groups on performance, (i.e., eyes open, eyes closed, firm, surface, foam surface), of the mCTSIB, $F(2, 30) = 2.81, p = .076, \eta_p^2 = .16$, or on displacement from the initial to the final position for the Fukuda Stepping Test, $F(2, 30) = 1.78, p = .186, \eta_p^2 = .11$. Of those participants who completed the mCTSIB 19% were characterized as falling or opening their eyes during the testing procedure, which included two YA, one CNOA, and five MCI participants. Table 3.1.1. shows the eyes closed, foam surface condition yielded more lower scores for all groups compared to mCTSIB conditions 1 – 3.
4. Discussion

The purpose of this study was to examine oculomotor and vestibular function in young adult, CNOA, and MCI groups. Oculomotor and vestibular function were assessed using VNG, VEMPs, mCTSIB, and Fukuda Stepping test. We hypothesized the young adult group would show better performance on measures of oculomotor and vestibular function compared to either CNOA or MCI groups. Findings showed shorter saccade latencies for young adults compared to either CNOA or MCI groups, but there were no group differences between CNOA or MCI groups. Results further showed significant group differences on VOR responsiveness suggesting a vestibular asymmetry for the MCI group. Overall, the MCI group showed greater mean caloric response ≥ 25% (on one side) compared to either YA or CNOA groups. The young adult group showed larger cVEMP P1-N1 peak amplitudes compared to either CNOA or MCI groups, but there were no differences between CNOA or MCI groups.

Table 3.8 Modified Clinical Test of Sensory Integration and Balance Performance

<table>
<thead>
<tr>
<th>Group</th>
<th>Eyes Open, Firm Surface M(SD)</th>
<th>Eyes Closed, Firm Surface M(SD)</th>
<th>Eyes Open, Foam Surface M(SD)</th>
<th>Eyes Closed, Foam Surface M(SD)</th>
<th>Total Score M(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YA</td>
<td>30.00 (0.00)</td>
<td>30.00 (0.00)</td>
<td>30.00 (0.00)</td>
<td>28.77 (3.36)</td>
<td>118.77 (3.36)</td>
</tr>
<tr>
<td>(n = 15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNOA</td>
<td>30.00 (0.00)</td>
<td>30.00 (0.00)</td>
<td>30.00 (0.00)</td>
<td>28.77 (4.44)</td>
<td>118.77 (4.44)</td>
</tr>
<tr>
<td>(n = 13)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCI</td>
<td>30.00 (0.00)</td>
<td>30.00 (0.00)</td>
<td>30.00 (0.00)</td>
<td>26.01 (6.65)</td>
<td>116.01 (6.65)</td>
</tr>
<tr>
<td>(n = 13)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

*p ≤ .05.

Table 3.9 Fukuda Stepping Test Group Performance

<table>
<thead>
<tr>
<th>Group</th>
<th>Displacement M(SD)</th>
<th>Turn &gt; 45° (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Open</td>
<td>Closed</td>
</tr>
<tr>
<td>YA</td>
<td>7.63 (6.78)</td>
<td>15.70 (9.10)</td>
</tr>
<tr>
<td>(n = 15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNOA</td>
<td>11.71 (8.99)</td>
<td>23.22 (12.00)</td>
</tr>
<tr>
<td>(n = 13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCI</td>
<td>14.98 (8.34)</td>
<td>22.70 (13.62)</td>
</tr>
<tr>
<td>(n = 13)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p ≤ .05.
Impaired VOR can result in oscillopsia, blurred vision when the head is in motion and objects appear to jiggle and bounce since they do not stay fixed at one point in the retina (Eckhardt-Henn et al., 2003) and abnormal nystagmus (Fife et al., 2000). Individuals with disrupted VOR are often experience difficulty reading during large or small active head or body movement (e.g., reading). Abnormal nystagmus may also blur vision as it causes excessive involuntary eye movements (Cha et al., 2009; Takahashi et al., 1990). VOR impairment may also lead to increased clumsiness, motion sickness, sensory issues and overall difficulty maintaining balance. If the sensory vestibular organs are not fully functional on either side, the brain will receive conflicting signals regarding movement, causing vertigo resulting in difficulty maintaining balance (Guinand et al., 2012; Kaminski & Leigh, 1997; Lambert et al., 2010), however, a single functional peripheral vestibular apparatus is not likely to result in significant functional balance impairment, spatial navigation impairment, or reduced hippocampal volume (Hüfner et al., 2007).

Unilateral vestibular asymmetry is a broad category of vestibular disorders defined by pathologic dysfunction of the VOR on one side. Caloric testing measures the function of the horizontal SCC and the pathway of the VOR. A caloric response is considered clinically significant if the response is reduced by ~ 25% or more one side. The VOR involves the peripheral sensory apparatus, a central processing mechanism, and oculomotor output (Fetter, 2007). The three SCCs provide sensory neural input regarding angular head acceleration, which is processed to coordinate compensatory eye and head movements via the VOR. The VOR originates from the SCCs of the inner ear to elicit compensatory eye movements and stabilize images on the retina during brief and rapid head rotation. When one labyrinth is stimulated (i.e., head motion, temperature) inhibition occurs on the side opposite the stimulation and eye
movements equal in speed and opposite the head movement are reflexively generated to stabilize the image on the retina while the head is in rotation (Fetter, 2007; Somisetty & Das, 2019). Information collected by first-order neurons, the peripheral vestibular sensory apparatus, regarding angular and linear acceleration and orientation of the head relative to gravity is transmitted to the second-order neurons of the vestibular nuclear complex located in the brainstem. Sensory information is further relayed to the central nervous system (CNS), the central processing mechanism that sends outputs to the spinal cord and ocular muscles to generate the VOR in response to SCC stimulation.

The present finding suggests older adults with MCI showed abnormal VOR responsiveness unilaterally, indicating deafferentation at the level of the peripheral apparatus. Anterograde degeneration, the destruction of lower structures which leads to degeneration of higher projection zones (Previc, 2013), presents a possible explanation for the present findings. Anterograde degeneration occurs following damage to sensory organs and can occur transneuronally with neurons several synapses removed from the affected sensory organ (Capurso et al., 1997). This suggests reduced neural activity at the level of the peripheral apparatus, however, degeneration would be expected to occur bilaterally rather than unilaterally. A second possible explanation for reduced VOR responsiveness for the MCI group includes central deafferentation beyond the peripheral apparatus, possibly involving the vestibular nuclei at the level of the brainstem representing an impairment of central transmission, reception, or integration of peripheral vestibular information. Cross-sectional and longitudinal studies have shown extensive white matter damage and more gray matter loss in parietal and frontal lobe regions compared to temporal and occipital lobe regions in healthy older adults (Courchesne et al., 2000; Resnick et al., 2003). Widespread white matter damage and gray matter loss are some
of the strongest cortical predictors of cognitive decline from mild to advanced stages of dementia, including the frontal, parietal and temporal and lobes (Brüggen et al., 2015; Du et al., 2001; Jack et al., 2000; Kitamura et al., 2013; Krasuski et al., 1998; Liu et al., 2013; McDonald et al., 2012; McEvoy et al., 2009; Nowrangi et al., 2013). Tissue loss in these regions may account for changes in central integration of sensory input from the peripheral vestibular apparatus (Jacobson et al., 2018). However, it is unlikely our result is due to reduced neural activity at or beyond the brainstem into higher projection areas (e.g., parieto-temporal lobe, medial temporal cortex, hippocampus) because a central abnormality would likely influence the self-perception of caloric stimulation rather than responsiveness of the VOR. The present finding is inconsistent with previous studies which have reported normal VOR responsiveness and caloric nystagmus in the presence of AD (Lakshminarayanan et al., 1986; Nakamagoe et al., 2015; Takemori & Ida, 1988), suggesting deafferentation and reduced neural activity expected in AD is unlikely to occur in the vestibular neural pathways (Nakamagoe et al., 2015).

Inconsistent with our hypotheses, the MCI group only showed reduced performance on the caloric subtest of the VNG battery which is a measure of VOR responsiveness often described as a unilateral vestibular asymmetry. Closer inspection of the individual caloric data showed SPVs within normal limits for all except (3) right cool and (6) left warm irrigations. Of the cool irrigations performed for the right ear, abnormal SPVs were obtained for one CNOA and two MCI participants. Of the warm irrigations performed for the left ear, abnormal SPVs were obtained for one YA, two CNOA and three MCI participants. Results also showed one participant from the MCI group had SPVs outside normal limits indicating a bilateral caloric weakness. Comparison of the individual caloric SPV data with the caloric weakness calculated
using computerized Chartr acquisition and analysis software suggests unilateral caloric weakness may not occur more frequently in older adults with MCI and may not differentiate older adults with and without MCI. Using this interpretation, our findings are consistent with the current literature on caloric weakness and cognitive decline.

An abnormal unilateral caloric weakness exists when the total responses from one ear are significantly weaker than the total responses from the opposite ear (Jacobson & Shephard, 2014). These cut-off values may differ between various normative datasets. Interpretation and clinical significance of unilateral weakness should include careful consideration of several factors. For example, unilateral caloric weakness is considered clinically significant when confined to one side, affecting one side more than the other. Conditions that affect both sides equally, such as aging, do not result in a significant unilateral weakness on the caloric test. A finding of unilateral caloric weakness can occur as a result of damage to the hair cells, vestibular nerve fibers, or blockage of the vestibular nerve at the root entry zone at the brainstem (Balogh & Honrubia, 2001), but unilateral caloric weakness cannot differentiate between damage to the hair cells and damage to the vestibular nerve fibers. A clinically significant finding is unlikely indicative of damage to the central vestibular pathways, unless it involves the root entry zone of the vestibulo-cochlear nerve (Uemura & Cohen, 1973). A clinically significant unilateral weakness must include substantial damage, at least 30 – 40%, to the hair cells in the horizontal SCC or the superior portion of the vestibular nerve to exceed normative values for unilateral caloric weakness. Hair cell damage can be caused by infection, trauma, and ischemia affecting the labyrinthine blood supply, toxic agents, and other causes such as metabolic disorder. Central nervous systems lesions can cause unilateral caloric weakness if they involve the root entry zone of the vestibulo-cochlear nerve. For example, participants with multiple sclerosis have shown
vestibular symptoms over the course of the disease (Aantaa et al., 1973; Dam et al., 1975; Prosser et al., 1989). This is likely due to demyelization which may cause disruption of neural transmission from the vestibular nerve to the central vestibular nuclei or other central structures. When the pathology is unilateral, irrigations will yield a clinically significant caloric weakness. It should be noted a finding suggestive of a CNS lesions rather than a peripheral vestibular lesion will show other central findings on the VNG test battery (Jacobson & Shephard, 2014).

Previous studies have examined the relationship between components of balance and cognitive decline; however, these studies used a variety of clinical measures to assess oculomotor and vestibular function, and an assortment of screening tools and tests to identify cognitive decline. This may be a contributing factor to the inconsistent findings in the literature. The present study examined both the oculomotor and vestibular contributions to balance. Our findings showed vestibular asymmetry characterized by reduced VOR, not otolith function, in a clearly defined group of older adults with MCI. Interestingly, Agrawal et al. (2012) also showed VOR function, assessed using vHIT, was impaired more often than otolith function, assessed using VEMPs, in older adults. However, head impulse testing is suggested to be a less accurate indicator of a pathologic process in individuals 70 years or older (Davalos-Bichara & Agrawal, 2014). The disparity in the reduction in hair cells in the vestibular periphery may account for these results. The otolith organs (i.e., saccule, utricle) undergo ~25% reduction of hair cells, while the SCCs undergo ~ 40% reduction in hair cells with age (Mathieson et al., 1999), which suggests the SCCs are more likely to be impaired with age compared to otolith organs. In addition, our findings showed no differences between groups on oVEMPs, which may result from the utricular hair cells susceptibility to age-related degeneration compared to saccular hair
cells (Gleeson & Felix, 1987), our small sample, size, or our broad age range of young adult participants.

The cVEMP amplitude findings showed the young adult group had larger P1-N1 amplitudes compared to both older adult groups; however, the average amplitude for both young and older adult groups was lower compared to other VEMP studies. For example, Piker et al. (2015) and Basta et al. (2007) report cVEMP amplitudes ranging from 73.8 – 212.1 microvolts in young adults age 20 – 40 years. Our results showed young adults 18 – 40 years had an average cVEMP of 19.04 microvolts. The present study also reported lower oVEMP amplitudes than expected for young adults based on previous work. Makowiec et al. (2017) reported N1-P1 peak-to-peak amplitudes of 12.42 microvolts in a group of 17 young adults (age: $M = 24.18$ years, $SD = 1.91$ years). In addition, Sandhu et al. (2013) reported oVEMP amplitudes, measured by the negative going peak at ~ 10 ms, of 5.67 microvolts in eight young adult participants age 22 – 36 years. Based on the results of Makowiec et al. (2017), we expected a combined belly-tendon, sitting approach would result in similar amplitudes of ~ 12 microvolts in young adult participants.

There were several limitations to the present study. The first limitation was the lack of comprehensive vestibular system function history. A previous injury or insult to the vestibular system may have caused a unilateral weakness or reduced VOR responsiveness to persist throughout the lifespan, possibly inflating the occurrence of unilateral weakness among the older adult MCI group for the present study. The second limitation includes the difference in VEMP amplitudes compared to previous studies. This difference may be due to differences our small sample size of both the present study and previous studies. In addition to a larger sample size, this study would have benefited from a pre-determined cut-off amplitude or voltage
for characterizing VEMP responses as present or absent. This information would help to examine the occurrence of VEMP responses in older adults with and without MCI. Differences on VEMP amplitudes and latencies in the present study compared to others may also be due to our characterization of the response. There are several approaches to describing the amplitude of the VEMP response, which can lead to inconsistencies in the VEMP literature with regard to how VEMP amplitude is recorded. For example, Sandhu et al. (2013) recorded oVEMP magnitude using the amplitude of the negative-going peak at ~10 ms. This variability, along with differences in age range, filter settings, and in hardware and software used for data collection may contribute to the range of VEMP amplitudes in the literature. Differences in stimulus intensity (Maleki et al., 2014; Welgampola & Colebatch, 2001) and stimulation frequency (Piker et al., 2013) can also lead to differences in VEMP amplitudes and latencies in the literature. Some may consider the small sample sizes associated with the Sandhu et al. (2013) and Makowiec et al. (2017) studies focused on optimal data acquisition to be too small to be considered representative of normative data with sample sizes of eight and 17 participants, respectively. This also highlights the need for normative VEMP data for young and older adults. While studies have reported normative VEMP data, is important to note to obtain stable estimates of population values, relatively large sample sizes must be employed.

Inconsistent with previous studies, the present study did not report any group differences on peak latencies for VEMP responses. Birdane et al. (2012) reported group differences on peak latency between cognitively impaired and control groups, however, participants with MCI and AD were part of the same participant group. The present study implemented a procedure for diagnosing MCI which included, comprehensive neuropsychological testing, and a physician’s exam. Our procedure for determining cognitive status, and our exclusion of participants with
probable AD as determined by the MoCA may have influenced our inconsistent findings compared to some previous studies. Studies using VEMPs to assess vestibular function in older adults with cognitive decline often included participants with only a confirmed diagnosis of AD (Harun et al., 2016), or combined participants with diagnoses of MCI and AD who were compared to controls as a single group (Birdane et al., 2012). In summary, sample size and differences in VEMP stimulus presentation level, stimulus type, transducer, and frequency along with characterization of VEMP amplitude and cognitive decline may have contributed to the differences in oculomotor and vestibular results observed between the present study and previous literature.

The present study used VNG to assess oculomotor and vestibular function which contribute to overall balance. The VNG battery is acknowledged as one of the most commonly used assessments of oculomotor and vestibular function, however, there are several limitations to this type of assessment. For example, VNG has limited ability to record subtle changes eye movements (e.g., torsional, rotary) due to slow camera speeds. Some saccadic eye movements may go undetected due to reduced camera speeds, which may influence the clinician’s interpretation of the oculomotor subtest data. In addition, the caloric subtest of the VNG battery only simulates head movement analogous to a speed of ~0.002 – 0.004 Hz, however, the vestibular system commonly responds to real-world head movements ranging from 1 – 6 Hz (Leigh & Zee, 2015; O'Leary, 1992). Therefore, results of the caloric subtest may not be an adequate real-world representation of VOR or vestibular function because a unilateral and bilateral vestibular asymmetry can exist in the presence of normal and symmetric caloric responses (Desmond, 2011). It is possible the occurrence of reduced VOR or vestibular asymmetry characterized by unilateral weakness may be higher than reported in the present
study. In addition, the caloric subtest of the VNG battery allows for testing of each horizontal SCC independent of the other, however, the evoked response can persist between irrigations. Persistence of the response between irrigations, duration of the test, and participant reactions during testing can make it difficult for serial or repeat testing of the caloric subtest.

VNG assessed the VOR at (low speeds), both horizontal SCCs, the otolith organs, and both branches of the vestibular nerve. A limitation of this study is incomplete assessment of the vestibular system. A comprehensive evaluation of the vestibular system should assess the functionality of the anterior and posterior SCCs, which can be achieved using video Head Impulse Testing (vHIT). Similar to the caloric subtest of the VNG battery, vHIT can assess each ear independent of the other, but unlike VNG, vHIT can assess all six SCCs. vHIT can assess functionality of the vestibular system at real-world high frequency speeds of 3 – 5 Hz. Unlike VNG, the stimulus does not persist between tests, the testing procedure is not taxing on the participant, and serial testing is possible. In addition, the time needed to perform vHIT testing is halved, and testing can be completed in the presence of a middle ear disorder or an ABG > 10 dB. It is possible that vHIT testing may yield more sensitive results as it is more representative of natural, realistic changes in head position compared to other measures of vestibular function.

5. Conclusion

The overall goal of this study was to identify elements of a clinical sensory-based protocol for use in distinguishing between older adults with and without MCI. The present findings do not provide compelling evidence in support of older adults with MCI, or cognitive decline, showing greater differences in oculomotor or vestibular function compared to older adults without MCI. Our findings suggest impaired VOR responsiveness assessed using caloric irrigations may provide pertinent information for distinguishing between older adults with and
without MCI, however, this result is not definitive. The relationship between balance and cognitive decline is worth exploring as a potential approach to early detection of cognitive decline. The impact of oculomotor and vestibular function on static and dynamic head and body movement, or functional balance, should be further investigated in a sample of older adults as a potential approach to the early detection of cognitive decline.
Chapter Two: Oculomotor and Vestibular Function, Functional Balance and Spatial Ability in Young and Older Adults

Abstract

Functional balance and spatial ability are known to be impaired in older adults with cognitive decline. The purpose of this study was to examine the relationships between oculomotor and vestibular function, functional balance, and spatial ability in young adults and older adults with and without MCI. Oculomotor and vestibular function, and cognitive status were assessed using screening and diagnostic measures. This data was collected and described in the previous study. Functional balance was assessed using the Timed Up and Go (Podsiadlo & Richardson, 1991) and Functional Reach tests (Duncan et al., 1990). Spatial ability was assessed using the Hidden Goal Task (Kalová et al., 2005), a computerized test of spatial navigation.

Forty-two participants comprised three groups (young adult, n = 15; CNOA, n = 13; MCI, n = 14). MANOVA was calculated to examine group differences on functional balance and spatial ability. Two multiple linear regressions were also calculated to examine the contribution of oculomotor or vestibular function to functional balance and spatial ability. The young adult group showed better performance on the Functional Reach and Timed Up and Go tests compared to MCI group, ps < .005, however, there were no differences between young adult and CNOA groups, ps > .114. The young adult group also showed better performance on the Hidden Goal Task compared to either CNOA or MCI groups, ps < .042. Results showed VOR and VSR were significantly associated with functional balance and spatial ability, respectively. These results
suggest VOR and VSR assessment may be considered as part of routine non-invasive battery for detecting signs and symptoms linked to cognitive decline, such as reduced functional balance and spatial ability.

1. Introduction

The nervous system is a complex collection of nerves and specialized neurons that transmit signals between the brain and different parts of the body. It is made up of two parts: 1) the peripheral nervous system (PNS) consisting of sensory organs, sensory neurons, ganglia, and nerves that connect to each other and to the CNS; and 2) the central nervous system (CNS), consisting of the brain and spinal cord. Sensory neurons react to physical stimuli such as light, sound, and touch, and send signals to the CNS regarding the body’s position and surrounding environment. The vestibular, visual, and somatosensory systems (parts of the PNS) each transmit sensory information regarding head and body position and physical awareness in space to the CNS. Integration of these multi-sensory signals is important for maintaining balance and physical awareness in space. With advancing age, there are several changes that occur in the peripheral and central nervous systems including, myelin loss, neuronal loss and atrophy of the brain (Andrews-Hanna et al., 2007; Bishop et al., 2010; Cabeza, 2002; Park & Reuter-Lorenz, 2009). These types of changes in the nervous system can degrade the sensory input, integration of sensory signals, and transmission of information to and from the brain.

Persons with cognitive impairment are at greater risk for balance and spatial orientation problems. Disorders of spatial orientation are considered an early symptom of cognitive impairment and are often attributed to hippocampal damage (Iachini et al., 2009). Abnormal neuronal loss and cerebral atrophy can cause problems with sensory processing and integration leading to impaired functional balance and spatial ability. Cross-sectional and longitudinal
imaging studies in healthy older adults have shown extensive white matter damage and gray matter loss in the parietal and occipital lobes (Courchesne et al., 2000; Resnick et al., 2003). Tissue loss in these regions may account for changes in central integration of sensory input. These white matter changes are also associated with decreased performance in cognitive functioning and changes in balance.

Older adults often report balance difficulty or unsteadiness, particularly when changing body positions or while walking (Alexander, 1994). Integrated static and dynamic movements (e.g., walking, reaching, etc.) that help to carry out activities of daily living are described as movements representative of functional balance. For example, walking or gait and reaching are important for carrying out activities of daily living, such as grocery shopping. Older adults’ gait is generally characterized by slower velocity, shorter step length, wider step width, and an increased proportion of time spent in the double support phase, when both feet are in contact with the ground (Sturnieks et al., 2008). Older also adults have increased difficulty controlling balance after perturbations, and increased difficulty incorporating avoidance of an obstacle (e.g., turning, sidestepping, stopping) into their normal gait patterns (Stelmach et al., 1989).

Balance difficulties are not a hallmark of aging. Balance problems can occur for multiple reasons including disruptions in one or more of the sensory systems (i.e., vestibular, visual, somatosensory) which contribute to balance and from inaccurate integration and central processing of information received from one or more of these sensory systems (Desmond, 2011). These types of changes can impact the ability to navigate through space and perform functional balance tasks, such as those needed to carry out activities of daily living (Salthouse & Somberg, 1982; Sturnieks et al., 2008). Functional balance and spatial awareness require a continuous representation of self-orientation, motion, and manipulation of visual representations within the
environment. To accomplish this, the central nervous system integrates afferent and efferent sensory information from the vestibular, visual, and somatosensory systems (Jacobson & Shephard, 2014); this integrated sensory information is further processed in specific regions of the brain (e.g., somatosensory, visual, and auditory) dedicated to processing sensory and motor neural signals. These neural signals are integrated and interpreted by the brain as head and body movements, and also transmit information regarding self-orientation (egocentric) and the relationships between objects (allocentric) in three-dimensional space (Moffat, 2009). This integrated sensory information directly contributes to maintaining balance and spatial awareness, executing purposeful movements, avoiding perturbations and successfully navigating through three-dimensional space (Angelaki & Dickman, 2019; Jacobson & Shephard, 2014; Moffat, 2009).

Balance and awareness in space are maintained by encoding and processing multi-sensory information from the visual, vestibular, and somatosensory systems. A failure in one of these systems will increase demand on those remaining to maintain balance. For example, when visual and somatosensory inputs become unreliable or unavailable, vestibular inputs become the most important for maintaining balance; the CNS can adapt by using visual and somatosensory inputs to compensate for the absence of vestibular input. Balance is often assessed using diagnostic tests of oculomotor or vestibular function, clinical tests of functional balance, or composite measures of balance. These types of tests are often administered by an audiologist or physical therapist, who specializes in one or more domains of balance assessment. A detailed description of commonly used screening and diagnostic measures used to assess oculomotor and vestibular components of balance are described in a previous study.
Balance and navigation problems can occur even in the early stages of cognitive impairment. Perception of motion, physical orientation, and awareness in space results from integrated multi-sensory information from visual, vestibular, and somatosensory signals which are processed in regions of the brain including the posterior parietal cortex, the hippocampus, and the parahippocampus. These brain regions are also part of a complex neural network for visuospatial processing, how the brain organizes and understands relations among objects in two- and three-dimensional space (Angelaki & Dickman, 2019). Abnormal age-related changes in the nervous system, such as those that occur in dementia, can severely disrupt the processing of sensory information essential to maintaining balance and negatively impacting functional balance and awareness of physical space (Angelaki & Dickman, 2019; Brandt et al., 2005).

Several studies provide evidence in support of a relationship between oculomotor and vestibular sensory function, spatial ability and cognitive decline. It is known that reduced hippocampal volume is associated with poorer navigation performance (Nedelska, 2012) and bilateral vestibular loss (Brandt, 2005). Peripheral vestibular sensory function assessed using cVEMPs has also been associated with poorer performance on measures of visuospatial ability (e.g., Cards Rotation (Ekstrom et al., 1976), Purdue Pegboard (Tiffin & Asher, 1948), Benton Visual Retention Test (Benton, 1945), and Trail Making Test (Reitan & Wolfson, 1985) in groups of participants with MCI and dementia (Bigelow et al., 2015). Similarly, Previc et al. (2014) reported VOR performance was associated with reduced spatial ability in a mixed group of older adults with and without MCI. Studies have also reported impaired spatial ability among older adults with varying degrees of cognitive status, including MCI and dementia measured using computerized, paper-pencil, and real-space measures of spatial ability (Hort et al., 2007; Kalová et al., 2005; Nedelska et al., 2012). It is important to note these studies assessed cognitive
decline and spatial ability using a wide variety of cognitive screening tools, neuropsychological assessments, and spatial tests (e.g., MoCA, MMSE, Wechsler Adult Intelligence Scale Revised [WAIS-R], and Wechsler Memory Scale Revised [WMS-R]).

Several studies have explored functional balance in older adult with and without cognitive decline, however, studies have primarily focused on dementia groups (Pettersson et al., 2002; Suttanon et al., 2012) with few studies on functional balance in well-defined MCI groups (Pettersson et al., 2005). Pettersson et al. (2002) and (Suttanon et al., 2012) reported older adults with dementia demonstrate poorer performance on measures of functional balance (e.g., the Functional Reach test, the Step Test, Timed Chair Stands, and the TUG test) compared to age and gender-matched controls. In a follow-up study, Pettersson et al. (2005) showed there were no group differences on performance on measures on functional balance (e.g., the Berg Balance Scale; Falls Efficacy Scale [FES]; the TUG test; Talking while Walking test [TWW]; and the Tinetti test) between older adults with and without MCI. In a similar study of older adult participants with MCI, dementia, and those without decline, Maquet et al. (2010) and Gillain et al. (2009) reported group differences between MCI and non-MCI groups on specific parameters of a gait task (i.e., stride frequency, step symmetry) used to assess functional balance. A limitation to these studies is the lack of a comprehensive evaluation of oculomotor and vestibular function which can help to enhance characterization of balance function profiles in older adults with and without cognitive decline. Additional limitations include a limited focus on balance performance between MCI and non-MCI groups, and well-defined MCI and non-MCI groups.

To date, few studies have comprehensively examined functional balance and its contributing sensory components (e.g., oculomotor function, vestibular function) in older adults with and without MCI, therefore, this relationship between cognitive decline and balance
function remains unclear. The contribution of visual, vestibular, and somatosensory systems to balance have been examined by manipulating sensory inputs and measuring the subsequent changes in balance. Little evidence has been found in support of associations between only decreased peripheral vestibular sensory acuity and chronic balance dysfunction (i.e., postural sway; Brocklehurst et al., 1982; Era & Heikkinen, 1985). Studies have reported visual, vestibular, and somatosensory inputs each as being associated with performance on balance outcomes. Lord and Menz (2000) and Colledge et al. (1994) reported visual inputs were strongly associated with performance on balance outcomes, however, Colledge et al. (1994) reported increased dependence on vision occurred only when somatosensory inputs became unreliable. In contrast, Lord et al. (1991) reported somatosensory function was a primary contributor to balance function, followed by visual and vestibular function. It should be noted that disruption to one of the major sensory inputs alone is generally not considered sufficient to assess the impact on balance function due to compensation by the remaining sensory courses; but disruptions to multiple sensory inputs that enable successful balance function will certainly yield a substantially greater effect (Teasdale et al., 1991). Generally, balance abnormalities due to unreliable sensory inputs are much greater in older adults compared young adults, suggesting less redundancy in the balance control systems (Fitzpatrick & McCloskey, 1994; Lord et al., 1991). It is important to understand how the multisensory function impacts overall functional outcomes (e.g., functional balance, spatial ability) in the presence of MCI in order to gain a more comprehensive understanding of a sensory profile or functional performance profile that may help to distinguish between MCI and non-MCI groups. A more focused investigation of these systems and processes will advance the field by further highlighting sensory or functional
outcomes that may be considered for inclusion in a clinical battery to facilitate the earlier detection of MCI.

The purpose of this study was to examine the relationships between oculomotor and vestibular function, functional balance, and spatial ability in young adults and older adults with and without MCI. Oculomotor and vestibular function data were collected and described in the previous study. Cognitive status was assessed using the MoCA coupled with standardized neuropsychological evaluations and a physician’s exam and was also described in detail in the previous study. Functional balance was assessed using the TUG (Podsiadlo & Richardson, 1991) and Functional Reach tests (Duncan et al., 1990). Spatial ability was assessed using the Hidden Goal Task ([HGT]; Kalová et al., 2005), a computerized test of spatial navigation. The secondary purpose of this study was to compare the contribution of peripheral vestibular sensory function to functional balance. We hypothesized young adults would demonstrate better performance on functional balance and spatial ability measures compared to either MCI or CNOA groups. Specifically, we expected the MCI group to show reduced functional reach displacement, slower walking speed performance, and more navigational errors compared to the CNOA group. We also hypothesized peripheral vestibular sensory function would be associated with functional balance and spatial ability for all groups.

2. Method

2.1 Participants

Forty-four participants were recruited and screened as part of the previous study. Informed consent was obtained for all potential participants. Older adult participants (n = 27) age 60 and older were recruited from the Keys to Staying Sharp randomized clinical trial (RCT, NCT03528486). Young adult participants were recruited from the Tampa Bay Area, including
the Department of Communication Sciences and Disorders at the University of South Florida. Inclusion criteria for the older adult group, per the *Keys to Staying Sharp* study, included a MoCA score ≥ 20, binocular near visual acuity of 20/50 or better, pure-tone thresholds <70 dB HL in the mid-frequency range (e.g., 1000, 2000 Hz) in at least one ear. Inclusion criteria for the present study included self-reported ability to rotate the head in the horizontal and vertical planes without discomfort. All eligible participants reported proficiency in the ability to speak, understand, and read English, and no history of neurological impairment. Additional inclusion and exclusion criteria are also detailed in a previous study. Forty-two participants were eligible for the present study: 15 young adult, 13 CNOA, and 14 older adults with MCI.

2.2 Measures

2.2.1 Hearing and Cognitive Function

All audiometric equipment was calibrated, properly functioning, and located in an environment free of electrical interference as specified in American National Standards Institute (ANSI) Standard s3.6 – 2010 (American National Standards Institute, 2010). Air conduction hearing thresholds were assessed at 500, 1000, 2000, 4000, 6000 and 8000 Hz using ER-30 insert earphones. Bone conduction thresholds were also assessed at 500 Hz. The MoCA (Nasreddine et al., 2005) and the Alzheimer’s Association/National Institute on Aging guidelines were used for the diagnosis or exclusion of dementia. Qualified psychometricians and clinicians administered these tests. Detailed descriptions of hearing and cognitive assessment are detailed in the previous study.
2.2.2 Balance Function

2.2.2.1 Peripheral Vestibular Sensory Function

All balance testing took place in the vestibular testing room at the University of South Florida Hearing Clinic. Oculomotor and vestibular sensory function were assessed using screening measures and clinical tests. Vestibular sensory function was assessed using the Fukuda Stepping Test (Fukuda, 1959), the modified Clinical Test of Sensory Integration and Balance ([mCTSIB]; Shumway-Cook & Horak, 1986; Wrisley & Whitney, 2004), VEMPs (Colebatch & Halmagyi, 1992; Colebatch et al., 1994). Both oculomotor and vestibular function were assessed using VNG (Glackin & Proctor, 1984; Proctor et al., 1981). Vestibular testing and recording parameters were completed and described as part of the previous study.

2.2.2.2 Functional Balance

The TUG test was used to examine participants’ functional balance (Rydwik et al., 2011; Shumway-Cook et al., 2000). Research has shown that the TUG predicts decline in activities of daily living (Lin et al., 2004), and functional balance (Podsiadlo & Richardson, 1991) among older adults. The TUG has also demonstrated good one-day intra-rater (Intra-class correlation coefficient = .92) and inter-rater reliability (Intra-class correlation coefficient = .91; Nordin, Rosendahl, & Lundin-Olsson, 2006). The Functional Reach test assessed postural control and static balance (Duncan et al., 1990). This test measured how far (in inches) participants were able to reach forward without moving the feet or becoming unsteady. The Functional Reach Test has demonstrated good construct validity and test-retest reliability, $r = .89$ (Duncan et al., 1990). Previous studies report a moderate to strong correlation between the TUG and Functional Reach tests (Bennie et al., 2003), therefore the functional balance outcome was a composite of the TUG test and the Functional Reach test.
2.2.2.3 Spatial Ability

The HGT is the computerized version of its real-space equivalent (Kalová et al., 2005). The HGT is designed to examine allocentric and egocentric navigation. Egocentric refers to the ability to navigate within an environment with reference to objects in space relative to the body axes (e.g., left-right, front-back, and up-down). Allocentric navigation refers to the ability to navigate within an environment with respect to other objects (e.g., landmarks) independent of the participant position.

2.3 Procedure

2.3.1 Functional Balance

For the TUG, participants were instructed to rise up from the seated position in an armed chair, walk 10 feet at their regular pace to a predetermined target, turn, walk back, and return to the seated position. Participants completed two trials of the task. The total time (in seconds) taken to complete each trial was averaged to compute a total TUG score. TUG scores > 12 seconds (s) were considered clinically significant for this study (Bischoff et al., 2003). The Functional Reach test participants were positioned next to the wall with one arm raised 90°. The distance in inches that a subject was able to reach forward from an initial upright posture to the maximal anterior leaning posture without moving or lifting the feet was measured by visual observation. The distances of two trials were averaged as the total score, with a greater distance indicating better balance ability. Functional Reach scores < 11inches were considered clinically significant for this study (Bohannon et al., 2017).

2.3.2 Spatial Ability

The HGT was performed using a computer monitor and mouse. The participant’s task was to locate an invisible goal in four different subtests that assess allocentric and egocentric
navigation, independently and combined. A large circle (280 pixels in diameter on a 640 x 480-pixel screen) will represent the arena participants will navigate. The goal was depicted by a small red circle inside the arena, with the starting point depicted as a circle on the arena contour, and orientation designated by red and green lines parallel to the arena contour. In the beginning of testing, the correct goal position and mutual relationship with the orientation cues is presented. Participants were instructed to remember the location of the goal by using its relationship to the starting position and the cues. Feedback is provided before the first trial of the task and after each trial. The goal then disappears, and the participant will use a computer mouse to draw the entire route from the start position to the target. There are eight trials in each subtest. Participants were reminded before each trial to locate the goal in a position relative to the start and orientation cues similar to the previous trials.

There was no time limit to locate the goal. After the participant indicates the supposed goal position, the correct position was displayed, and participants are prompted to note the relative position to the starting position and cues. In the first subtest of combined allocentric and egocentric navigation, both the start-goal relationship and the relative positions of the two orientation cues were displayed to help locate the goal. In the second egocentric subtest, only the starting position was displayed to help locate the goal. In the third allocentric subtest, the two orientation cues at the arena periphery were displayed for navigation. This time, however, each trial started from a different starting location relative to the goal. The fourth subtest consisted of only two trials administered 30 minutes following subtest three. The purpose of this subtest was to measure the effect of time delay. For the computerized version of the HGT, the average distance error was measured in pixels (Nedelska et al., 2012). The total average distance error across eight trials was calculated for each participant.
2.4 Data Analysis

MANOVA was calculated to examine group differences on education and hearing. Chi-square analyses were calculated to examine the relation between MCI, race, and sex. Several additional analyses were calculated to: 1) examine relationships between oculomotor, vestibular (e.g., mCTSIB, Fukuda, VEMP, VNG) functional balance and spatial ability measures; 2) compare groups on measures of functional balance and spatial ability; 3) examine the contribution of oculomotor or vestibular function to functional balance or spatial ability; and 4) examine the proportion of participants with clinically significant caloric unilateral weakness and abnormal functional balance (see Table 4).

To create a functional balance composite, raw scores for the TUG and Functional Reach tests were transformed to z-scores. For the TUG test, a lower score represents better performance, therefore, TUG scores were reverse scored (multiplied by -1). The transformed z-scores were added together to create a functional balance composite. Pearson r correlations showed caloric unilateral weakness, saccade latency, and the Fukuda Stepping test had correlations with HGT, ranging from .209 – .296. Similarly, Pearson r correlations showed mCTSIB, OKN gain asymmetry, gaze, and caloric unilateral weakness had correlations with Functional Reach ranging from .257 – .347. Alpha values were set to .05. Post hoc examinations of significant findings were conducted using LSD corrections. Means substitutions were used and effect sizes are reported as partial eta squared ($\eta^2_{p}$).
Table 4 Functional Balance and Spatial Ability Analyses

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson correlation</td>
<td>To examine relationships between oculomotor, vestibular, functional balance and spatial ability measures.</td>
</tr>
<tr>
<td>MANOVA</td>
<td>To compare groups on measures of functional balance and spatial ability.</td>
</tr>
<tr>
<td>Linear regression</td>
<td>To examine the contribution of oculomotor or vestibular function to: 1) functional balance; and 2) spatial ability.</td>
</tr>
<tr>
<td>Chi-square</td>
<td>To compare the proportion of participants with unilateral caloric weakness and abnormal functional balance.</td>
</tr>
</tbody>
</table>

*Note. MANOVA = Multivariate Analysis of Variance*

3. Results

3.1 Balance Function

Group demographics were reported in the previous study and presented in Table 1. MANOVA was calculated to compare groups on measures of functional balance. No significant effect was found, Wilks’ Lambda = .581, $F = (12, 66) = 1.72$, $p = .083$, $\eta^2_p = .24$. However, the purpose of this study was to examine functional balance among groups and follow-up univariate tests are reported below. There were significant group differences for the Functional Reach, $F(2, 38) = 4.64$, $p = .016$, $\eta^2_p = .196$, and TUG, $F(2, 38) = 6.47$, $p = .004$, $\eta^2_p = .254$, tests. LSD post-hoc analyses showed the young adult group yielded greater displacement on the Functional Reach test compared to the MCI group, $p = .005$, however, there were no group differences on displacement between either young adult or CNOA groups, $p = .337$, or between CNOA or MCI groups, $p = .067$. For the TUG test, LSD post-hoc analyses showed the young adult group had faster completion times compared to the MCI group, $p = .001$. There were no group differences found between young adult or CNOA groups, $p = .114$. In addition, there were no group differences between CNOA or MCI groups, $ps = .079$.

Chi-square analyses were calculated to examine the proportion of abnormal functional balance and unilateral caloric weakness between groups. A significant interaction was found, $X^2 = 15.59$, $p = .000412$. The MCI group showed the highest proportion of abnormal functional
balance and unilateral caloric weakness (69.2 \%). Finally, a multiple linear regression was calculated to examine the contribution of oculomotor or vestibular function to functional balance. The regression equation was significant, \( F(1, 36) = 4.92, p = .033 \), with an \( R^2 \) of .120. Caloric weakness was a significant predictor of functional balance and accounted for 12\% of the variance.

Table 5 Functional Balance Group Performance

<table>
<thead>
<tr>
<th>Group</th>
<th>TUG M(SD)</th>
<th>Functional Reach M(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YA</td>
<td>10.22*</td>
<td>12.68*</td>
</tr>
<tr>
<td>(n = 15)</td>
<td>(2.06)</td>
<td>(1.78)</td>
</tr>
<tr>
<td>CNOA</td>
<td>11.29</td>
<td>11.67</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(1.27)</td>
<td>(2.53)</td>
</tr>
<tr>
<td>MCI</td>
<td>12.50</td>
<td>9.69</td>
</tr>
<tr>
<td>(n = 14)</td>
<td>(1.59)</td>
<td>(3.46)</td>
</tr>
</tbody>
</table>

*Note. TUG = Timed Up and Go; CNOA = Cognitively Normal Older Adult; MCI = Mild Cognitive Impairment.
*p ≤ .05.

3.2 Spatial Ability

There were significant group differences for the Allo, \( F(2, 38) = 3.70, p = .034, \eta^2_p = .163 \), and AlloEgo, \( F(2, 38) = 3.83, p = .031, \eta^2_p = .168 \), subtests, and total error across all subtests of the HGT, \( F(2, 38) = 3.26, p = .049, \eta^2_p = .146 \). LSD post-hoc analyses showed the young adult group yielded fewer navigation errors compared to either CNOA or MCI groups on the Allo, AlloEgo subtests, and total error across all subtests, \( ps < .042 \). However, there were no group differences on spatial navigation error between either CNOA or MCI groups, \( ps = .947 \). This finding highlights the effect of age on spatial ability. In addition, there were no group differences on navigation error on the Ego, \( F(2, 38) = .426, p = .656, \eta^2_p = .022 \), or Delayed, \( F(2, 38) = 1.55, p = .226, \eta^2_p = .075 \), subtests of the HGT. A multiple linear regression was calculated to examine the contribution of oculomotor or vestibular function to spatial ability. The regression equation was significant, \( F(1, 37) = 4.70, p = .037 \), with an \( R^2 \) of .11. Performance on the Fukuda
Stepping test was a significant predictor of spatial ability and accounted for 11% of the variance on spatial ability.

**Table 6 Spatial Navigation Group Performance**

<table>
<thead>
<tr>
<th>Group</th>
<th>Allo M(SD)</th>
<th>Ego M(SD)</th>
<th>AlloEgo M(SD)</th>
<th>Delayed M(SD)</th>
<th>Total Error M(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YA (n = 15)</td>
<td>25.55* (13.36)</td>
<td>42.13 (33.78)</td>
<td>26.81* (17.26)</td>
<td>24.94 (15.77)</td>
<td>119.43* (68.51)</td>
</tr>
<tr>
<td>CNOA (n = 13)</td>
<td>44.72 (24.48)</td>
<td>51.88 (19.81)</td>
<td>50.34 (31.26)</td>
<td>42.36 (38.54)</td>
<td>189.30 (91.67)</td>
</tr>
<tr>
<td>MCI (n = 14)</td>
<td>42.18 (19.32)</td>
<td>49.47 (27.64)</td>
<td>46.38 (18.86)</td>
<td>41.03 (25.15)</td>
<td>179.05 (60.58)</td>
</tr>
</tbody>
</table>

*Note. Allo = Allocentric; Ego = Egocentric; AlloEgo = Allocentric and Egocentric.

*p ≤ .05.

**4. Discussion**

The purpose of this study was to compare the contribution of peripheral vestibular sensory function to spatial ability and functional balance. We hypothesized young adults would demonstrate better performance on measures used to assess balance and spatial ability compared to MCI or CNOA groups. We also hypothesized that peripheral vestibular sensory function would be a significant predictor of functional balance and spatial ability. Inconsistent with our hypotheses, results indicated the young adult group showed greater displacement on the Functional Reach test and faster completion times on the TUG test compared only to the MCI group. There were no group differences on functional balance between young adult and CNOA groups. Results of the spatial ability task were however in line with our hypotheses, with the young adult group demonstrating better performance compared to either CNOA or MCI groups. Performance on the spatial ability task did not differ between either CNOA or MCI groups. In line with our hypotheses, peripheral vestibular sensory function, specifically VOR and VSR, was significantly associated with functional balance and spatial ability, respectively.
The literature regarding functional balance in older adults with and without MCI remains unclear. Consistent with other studies that have examined functional balance among older adults with MCI our results indicate functional balance performance does not differ between older adults with and without MCI (Gillain et al., 2009; Mirelman et al., 2014; Pettersson et al., 2005; Shin et al., 2011). In contrast, other studies using other measures of functional balance have reported differences on performance between MCI and non-MCI groups (Aggarwal et al., 2006; Franssen et al., 1999; Leandri et al., 2009). Inconsistencies in the literature may be due to the wide variety of terms and measures used to describe and characterize balance function. Mixed findings may be due to lack of well-defined patient groups and differences in classification of MCI. In consideration of prior studies that report differences between MCI and non-MCI groups, our results suggest characterization of overall performance, specifically on the TUG and Functional Reach tests, may lack sensitivity needed to detect differences between groups. A more detailed characterization of functional balance including assessment of postural sway or gait pattern, similar to that of Mirelman et al. (2014), (Gillain et al., 2009) or Leandri et al. (2009) may be needed to distinguish between older adults with and without MCI. However, more detailed characterization of functional balance may be accompanied with concerns of accessibility and feasibility.

The contribution of visual, vestibular, and somatosensory systems to balance has been examined by manipulating sensory inputs and measuring the subsequent changes in balance (e.g., postural sway, small deviations in center of mass position). Little evidence has been found in support of associations between only decreased peripheral vestibular sensory acuity and chronic balance dysfunction (i.e., postural sway; Brocklehurst et al., 1982; Era & Heikkinen, 1985). Our results suggest peripheral vestibular sensory function (i.e., VOR, VSR) was
associated with performance on measures of balance. Previous studies have reported visual, vestibular, and somatosensory inputs each as being associated with performance on balance outcomes. Lord and Menz (2000) and Colledge et al. (1994) reported visual inputs were strongly associated with performance on balance outcomes, however, Colledge et al. (1994) further reported increased dependence on vision occurred only when somatosensory inputs became unreliable. In contrast, Lord et al. (1991) reported somatosensory function was a primary contributor to balance function, followed by visual and vestibular function, however, a significant amount of variance remained unexplained. As previously mentioned, it should be noted that disruption to one of the major sensory inputs alone is generally not considered sufficient to assess the impact on balance function due to compensation by the remaining sensory courses; but disruptions to multiple sensory inputs that enable successful balance function will certainly yield a substantially greater effect (Teasdale et al., 1991). Generally, balance abnormalities due to unreliable sensory inputs are much greater in older adults compared young adults, suggesting less redundancy in the balance control systems (Fitzpatrick & McCloskey, 1994; Lord et al., 1991). Stelmach and Worringham (1985) suggest that deterioration of central integrative processes may further explain decreased balance function observed in the older adult population.

Our findings indicate vestibular function, not visual or somatosensory function, was most associated with performance on measures that assess functional balance. These results may be due to disparities in our assessment of visual and somatosensory inputs that contribute to balance. A limitation to the present study was our assessment of the impact of the removal of visual and somatosensory cues on balance. While, our assessment of oculomotor and vestibular function was comprehensive, with the exception of anterior and posterior SCC assessment, our
assessment of how balance was impacted when visual and somatosensory cues were removed was lacking. Our use of a screening tool, the mCTSIB, rather than a more comprehensive assessment of how balance was impacted when visual and somatosensory cues were removed (e.g., Sensory Organization Test) may have contributed to findings in the present study.

Vestibular function was also associated with spatial ability which is a process known to be impacted in unilateral (Chapuis et al., 1992) or bilateral peripheral vestibular impairment (Brandt et al., 2005). The young adult group completed the HGT with fewer errors, but there were no differences between CNOA and MCI groups. This finding indicates there was no peripheral vestibular impairment among either of the three groups, and our findings is the result of an overall age effect.

As previously mentioned, a limitation of the present study was the limited objective characterization of participants’ gait and stepping pattern. While this study implemented commonly used clinical assessments of gross functional balance, inclusion of more objective measures for characterizing gait and balance, such as the OptoGait system (Lee et al., 2014), may prove a more sensitive and analytic method of assessing functional balance in young and older adult groups and distinguishing between older adults with and without MCI. The OptoGait system consists of a transmitting and receiving bar positioned on the sides of a treadmill. OptoGait software obtains parametric data throughout the gait cycle including step length, stance phase, swing phase, single support, double support, load response, and swing phase. Several studies have demonstrated that OptoGait is reliable, accurate, and a valid tool for gait analysis (Lee et al., 2014; Lienhard et al., 2013). Previous research has demonstrated high discriminant and concurrent validity of the OptoGait system for the assessment of spatiotemporal gait parameters (Lienhard et al., 2013). Another limitation of the present study may have been related
to the simplicity of the functional balance tasks implemented and our method for assessing performance (e.g., completion time). Perhaps implementation of a dual-task functional balance measure may have proven more sensitive for distinguishing between MCI and non-MCI groups.

Difficulties with functional balance and spatial ability may manifest due to reduced ability to integrate multi-sensory information memory, suggesting a central processing deficit. It is also possible that reductions in peripheral and central processing occur concurrently, further increasing balance difficulty. To further examine central integration of sensory information, future studies should focus on the association between the absence of caloric perception and functional balance. In addition, future studies should incorporate dual-task assessments and comprehensive gait characterization into a balance assessment protocol to gain further insight into balance differences between MCI and non-MCI groups. Future models of balance should include comparable assessment of visual, vestibular, and somatosensory inputs, both peripheral and central vestibular processing components, cognitive factors (e.g., problem-solving, attention, processing speed), and functional balance.

5. Conclusion

Low recognition of cognitive decline may be due to several barriers including infrequent use of available cognitive screening tools and limited inter-professional involvement in the early detection of cognitive decline (Cordell et al., 2013; Galvin & Sadowsky, 2012). The overall goal of this study was to examine functional balance and spatial ability in older adults with and without MCI. Our results showed young adults performed better on measures of functional balance and spatial ability compared to either CNOA or MCI groups. There were no group differences between CNOA and MCI groups. Our results provide evidence in support of the contribution of vestibular function to functional balance and spatial ability. Our results also
highlight the need for detailed analysis of functional balance performances to potentially distinguish between MCI and non-MCI groups.
Overall Discussion and Conclusion

Cognitive screenings and neuropsychological evaluations are underused, and early detection of cognitive decline is underreported. Routine sensory function assessment may prove a potential interdisciplinary approach to enhancing traditional approaches to early detection of cognitive decline. This dissertation detailed two pilot studies focused on developing elements of a battery aimed to examine balance function as a potential early indicator of cognitive decline, specifically MCI. We examined oculomotor and vestibular function, functional balance, and spatial ability in young adult, CNOA, and MCI groups. We hypothesized the young adult group would show better performance on measures of oculomotor and vestibular function compared to either CNOA or MCI groups. We also hypothesized vestibular function would be significantly associated with measures of functional balance and spatial ability.

Findings showed shorter saccade latencies for young adults compared to either CNOA or MCI groups, but there were no group differences between CNOA or MCI groups. Results further showed significant group differences on VOR responsiveness suggesting a clinical vestibular asymmetry for the MCI group compared to either young adult or CNOA groups, however, closer investigation of the individual data indicate bithermal caloric SPV values within clinically normal limits for all groups. For vestibular function the young adult group showed larger cVEMP P1-N1 peak amplitudes compared to either CNOA or MCI groups, but there were no differences between CNOA or MCI groups. Similarly, the young adult group demonstrated better performance on the measures of functional balance and spatial ability compared to either CNOA or MCI, groups with no group differences on performance between CNOA or MCI.
groups. Collectively, our results provide evidence in support of associations between vestibular function, functional balance, and spatial ability. Our results highlight the need for more detailed analysis of functional balance performances to potentially distinguish between MCI and non-MCI groups. This study also helped to streamline a potential protocol for assessment of oculomotor peripheral vestibular function for future studies seeking to further examine relationships between the various systems contributing to overall balance.

There were several limitations to these studies including limited analytic characterization of measures of functional balance. Previous studies reporting differences on performance between MCI and non-MCI groups obtained such results by analyzing several parameters of measures of functional balance rather than analyzing simple overall performance (e.g., completion times). Another limitation to the present study includes our small sample size which may have also contributed to several of our null findings. In addition, disparities in our assessment of vestibular, oculomotor, and somatosensory function may have influenced our findings. For example, compared to oculomotor and vestibular function were assessed using comprehensive evaluation tools, whereas, somatosensory function was assessed using a single clinical screening tool. It is possible such a vestibular heavy battery may have influenced our significant vestibular findings. While the oculomotor and vestibular portions of the battery were more comprehensive, it should be noted the battery lacked assessment of the anterior and posterior SCCs.

These studies further highlight the potential for interprofessional practice to facilitate early detection of cognitive decline. There is a need to equip health care professionals with various subspecialties to promote the immediate referral of high-risk older adults for thorough cognitive assessment. Declines in sensory and motor function are known to occur several years
before symptoms of cognitive decline appear, however it is unclear which sensory and/or motor system(s) best distinguishes between older adults with and without MCI. Previous work has investigated associations with decline in sensory function and MCI within the scope of practice of clinical audiology, including the P1-N1-P2 complex (e.g., Bidelman et al., 2017; Li et al., 2016; Lister et al., 2016) and central auditory processing measures (Edwards et al., 2017; Gates et al., 1995; Idrizbegovic et al., 2013; Rahman et al., 2011). Specifically, studies have reported difference in P1, P3, and P3b amplitudes and latencies between MCI and non-MCI groups compared to healthy controls (Golob et al., 2002; Irimajiri et al., 2005; Lister et al., 2016). Lister et al. (2016) showed older adults with probable MCI (defined using the MoCA) yielded larger P2 amplitudes for non-MCI compared to this with probable MCI with a large effect size, \( p = .006, \eta^2_p = .239 \). In a behavioral study, Edwards et al. (2017) showed older adults with probable MCI (defined using the MoCA) yielded significant group differences on measures of central auditory processing (i.e., Synthetic Sentence Identification with Ipsilateral Competing Message, Dichotic Sentence Identification, Adaptive Tests of Temporal Resolution within channel) compared to non-MCI groups, again with medium to large effect sizes, \( \eta^2_p = .03 \text{ -- } .24 \). While the results of these studies remain inconclusive, future studies should continue to explore associations with decline in sensory function and functional abilities, such as balance, and MCI within the scope of practice of clinical audiology and other inter-professional practices. Ongoing research should seek to identify a comprehensive inter-professional practice protocol to facilitate early detection of cognitive decline. Further research is needed to refine, validate, and standardize, such protocols before they are ready for general clinical practice. Studies may also consider investigating the potential for telehealth services and technologies devices to further facilitate inter-professional practices to help detect cognitive decline.
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In.


Angelaki, D., & Dickman, J. D. (2019). *The vestibular system*. Champaign, IL.


**Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology, 37(8), 1137.**


Interference between postural control and mental task performance in patients with


Appendix I

May 16, 2019

Diana Julbe-Delgado
Communication Sciences and Disorders
4202 E. Fowler Avenue
PCD 2000A
Tampa, FL 33620

RE: Expedited Approval for Initial Review
IRB#: Pro00040303
Title: Language and Balance: Indicators of Mild Cognitive Impairment

Study Approval Period: 5/15/2019

Dear Mrs. Julbe-Delgado:

On 5/15/2019, the Institutional Review Board (IRB) reviewed and APPROVED the above application and all documents contained within, including those outlined below. **Please note this study is approved under the 2018 version of 45 CFR 46 and you will be asked to confirm ongoing research annually in place of a full Continuing Review. Amendments and Reportable Events must still be submitted per USF HRPP policy.**

Approved Item(s):
Protocol Document(s):
 Protocol, Version #1, 05/13/19

Consent/Assent Document(s)*:
 Adult Consent, Version #1, 05/13/19.pdf
 Telephone Screening, Version #1, 05/13/19

*Please use only the official IRB stamped informed consent/assent document(s) found under the "Attachments" tab. Please note, these consent/assent documents are valid until the consent document is amended and approved. The Telephone Screening form is not a stamped form. It was the determination of the IRB that your study qualified for expedited review which includes activities that: (1) present no more than minimal risk to human subjects, and (2) involve
only procedures listed in one or more of the categories outlined below. The IRB may review research through the expedited review procedure authorized by 45 CFR 46.110. The research proposed in this study is categorized under the following expedited review category:

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing.

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Your study qualifies for a waiver of the requirements for the documentation of informed consent as outlined in the federal regulations at 45 CFR 46.117(c), which states that an IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds any of the following: (1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; (2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or (3) if the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm provided that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. (Telephone screening consent form).

As the principal investigator of this study, it is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB. Any changes to the approved research must be submitted to the IRB via an Amendment for review and approval. Additionally, all unanticipated problems must be reported to the USF IRB within five (5) business days.

We appreciate your dedication to the ethical conduct of human subjects research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

[Signature]

Kristen Salomon, Ph.D., Chairperson
USF Institutional Review Board