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Epidemiology of Vestibular Evoked Myogenic Potentials: Data from the Baltimore Longitudinal Study of Aging

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Abstract

Objective—To evaluate whether age-related changes in vestibular evoked myogenic potentials (VEMPs) differ by demographic and cardiovascular risk groups.

Methods—Participants in the Baltimore Longitudinal Study of Aging underwent cervical and ocular VEMP testing. VEMP latency, amplitude, asymmetry ratios, and prevalence of absent responses were compared across demographic and cardiovascular risk groups.

Results—In 257 participants (mean age 72.9, 57% female), ocular VEMP (oVEMP) n10 latency increased by 0.12 ms/decade while amplitude decreased by 2.9 μV/decade. Black participants had better oVEMP function (shorter latency, increased amplitude, and decreased odds of absent responses) relative to white participants. In 250 participants (mean age 72.6, 54% female), EMG-corrected cervical VEMP (cVEMP) amplitude decreased by 0.14 μV /decade and p13 latency was 0.38 ms longer in males. The odds of absent responses were significantly higher in individuals age ≥ 80 for oVEMPs, and age ≥ 70 for cVEMPs. Cardiovascular risk factors had no association with VEMP parameters.

Conclusions—We confirmed age-related declines in otolith function, and observed a protective effect of black race on oVEMP latency and amplitude.

Significance—These results illustrate how measures of otolith function change with age in community-dwelling adults. Further investigations are needed to ascertain whether better otolith function in blacks might contribute to a lower risk of mobility disability and falls.

Keywords

Vestibular evoked myogenic potential; vestibular; aging

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Conflict of Interest None of the authors have potential conflicts of interest to be disclosed.

Introduction

The human vestibular system, integral to balance control, is composed of three semicircular canals that detect angular acceleration and two otolith organs, the utricle and saccule, which detect linear acceleration. Epidemiologic analyses of data from the National Health and Nutrition Examination Survey (NHANES) found a 35% prevalence of vestibular impairment in over 5000 US adults age ≥ 40, and the prevalence was found to increase steeply with age (Agrawal et al., 2009). Additionally, odds of vestibular impairment were 70% higher in individuals with diabetes mellitus. Vestibular impairment in NHANES was defined as the inability to maintain balance on a foam-padded surface with eyes closed for 30 seconds (Agrawal et al., 2009). Although this study provides strong epidemiologic support for a loss of vestibular function associated with aging, the postural tests used in NHANES are limited in the specificity with which they measure vestibular function, given that performance on these tests also relies on other sensory inputs, central processes, and motor function.

Tests that more specifically measure vestibular function include vestibular evoked myogenic potentials (VEMPs), which are increasingly being used to evaluate otolith function. Cervical VEMPs (cVEMPs) in response to air-conducted sound have been shown to reflect the integrity of the saccule and inferior vestibular nerve, while ocular VEMPs (oVEMPs) in response to midline tap vibration have been shown to reflect the integrity of the utricle and superior vestibular nerve (Rosengren et al., 2011, Kantner et al., 2012). Several studies have provided normative data for VEMPs elicited by various air-conducted and midline tap stimuli (Welgampola et al., 2001, Basta et al., 2005, Brantberg et al., 2007, Singh et al.), and have begun to characterize age-related changes in VEMP parameters and tuning properties (Piker et al., Welgampola et al., 2001, Zapala et al., 2004, Brantberg et al., 2007, Janky et al., 2009, Rosengren et al., 2011, Kantner et al., 2012, Taylor et al., 2012, Singh et al., 2013). Although age has been shown to have a significant impact on VEMP responses, the effect of other demographic characteristics and cardiovascular risk factors has not been established.

In this study, we evaluated cVEMPs and oVEMPs in a large cohort of community-dwelling individuals across the age range from 26 to 92 years. We performed VEMP testing with air-conducted sound and midline tap stimuli and evaluated changes in VEMP latency, amplitude and asymmetry ratio as a function of age, sex, and race. Given previous findings of an association between vestibular impairment and diabetes mellitus (Agrawal et al., 2009), we also examined the relationship between VEMP parameters and cardiovascular comorbidities such as hypertension, diabetes mellitus, hyperlipidemia, and smoking status. We anticipate that this observational epidemiological study will provide an estimate of the magnitude of otolith dysfunction in community-dwelling older individuals and its distribution in the US population.

Methods

Subjects

The Baltimore Longitudinal Study of Aging (BLSA) is an ongoing prospective cohort study initiated by the National Institute on Aging (NIA) in 1958. Subjects consist of community-

dwelling participants who travel to the NIA for 2.5 days of comprehensive testing. Ocular and cervical VEMP testing were added to the test protocol in February 2013. Individuals were excluded from oVEMP testing if they could not participate in the protocol because of blindness. Individuals were excluded from cVEMP testing if they had a history of conductive hearing loss and/or could not move their neck without restriction or pain. From February to December 2013, 314 participants completed one study visit, of whom 257 completed ocular VEMP testing and 250 completed cervical VEMP testing. Of the participants who did not undergo oVEMP testing, 31 individuals were not tested due to time constraints and/or tester unavailability, 5 individuals were ineligible according to exclusion criteria, and 21 individuals were unable to complete testing due to technical difficulties. Of the participants who did not undergo cVEMP testing, 31 individuals were not tested due to time constraints and/or tester unavailability, 11 individuals were ineligible according to exclusion criteria, and 22 individuals were unable to complete testing due to technical difficulties. Technical difficulties included mechanical and recording problems associated with the EMG system and not the subject. Tested vs. untested participants did not differ significantly by age, gender or race. Demographics (including gender and race), cardiovascular risk factor data, and smoking history were collected from extensive subject interviews. Participants were asked to designate a race from the following options: White, Black or African Americans, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, “Two or More Races”, “Don’t Know”, and “Refused”. History of hypertension was assessed with the question, “Has a doctor or other health professional ever said you had high blood pressure or hypertension?” History of diabetes mellitus was assessed with the question, “Has a doctor or other health professional ever said you had diabetes, glucose intolerance, or high blood sugar?” History of hyperlipidemia was assessed with the question, “Has a doctor or other health professional ever said you had high cholesterol, triglycerides, dyslipidemia, or hypercholesterolemia?” History of smoking was assessed by asking participants “Have you smoked at least 100 cigarettes over your entire life,” “Have you smoked at least 50 cigars over your entire life,” and “Have you smoked at least 3 packages of pipe tobacco over your entire life?” All participants provided written informed consent, and the BLSA study protocol was approved by the Institutional Review Board associated with the BLSA at Harbor Hospital in Baltimore, MD.

Vestibular Evoked Myogenic Potential Recording Conditions

A commercial eletromyographic (EMG) system (Carefusion Synergy, software version 14.1, Dublin, OH, USA) was used. EMG signals were recorded with disposable, self-adhesive, pregelled, Ag/AgCl electrodes with 40-inch safety leadwires from GN Otometrics (Schaumburg, IL, USA). EMG signals were amplified 2500x and band-pass filtered, 20-2000 Hz for cVEMPs, 3-500 Hz for oVEMPs (Nguyen et al., 2010).

Ocular Vestibular Evoked Myogenic Potential Testing

Subjects laid with upper bodies elevated at 30° from horizontal. The skin overlying both cheeks and the manubrium sterni was cleansed with alcohol preps before electrode placement. A noninverting electrode was placed on the cheek approximately 3 mm below the eye, directly beneath the pupil, an inverting electrode was placed 2cm below the noninverting electrode and a ground electrode was placed on the manubrium sterni. Before

stimulation, participants were instructed to perform 20-degree vertical saccades to ensure that symmetrical signals were recorded from both eyes. In the experimental set-up, the participant's eye level is marked on the wall next to the participant's chair and targets on the ceiling were measured and marked to elicit the 20-degree vertical saccades with the participant's eyes at the specified level. If signals showed greater than 25% asymmetry, the electrodes were removed and new ones applied. Participants were instructed to maintain a 20° upgaze during oVEMP stimulation and recording.

Midline vibration stimuli consisted of head taps delivered manually with an Aesculap model ACO12C reflex hammer fitted with an inertial microswitch trigger. Head taps were delivered at Fz, in the midline at the hairline, 30% of the distance between the inion and nasion. Fifty sweeps for head taps were averaged for each test.

Cervical Vestibular Evoked Myogenic Potential Testing

Participants laid with upper bodies elevated at 30° from horizontal. The skin overlying both sternocleidomastoid (SCM) muscles and the manubrium sterni was cleansed with alcohol preps before electrode placement. A noninverting electrode was placed at the midpoint of the SCM muscle, an inverting electrode was placed on the sternoclavicular junction, and a ground electrode was placed on the manubrium sterni. Participants were instructed to lift their heads up from the head rest to provide tonic background SCM activity during stimulation and recording, and a pre-stimulus rectifying surface EMG signal of at least 30 microvolts over 10 ms was required for accepting a cVEMP tracing.

Air-conducted sound stimuli consisted of 500 Hz, 125 dB SPL tone bursts of positive polarity, with a linear envelope (1ms rise/fall time, 2 ms plateau), at a repetition rate of 5 Hz. Sound stimuli were delivered monaurally through Audiocups, noise-excluding headset enclosures from Amplivox (Eden Prairie, MN, USA).

Response parameters

The oVEMP waveform consists of a negative peak (n10), identified as the first distinctive peak in the waveform, followed by a positive peak (p16), identified as the first distinctive trough in the waveform. Subjects with EMG recordings lacking definable n10 waves were defined as having an absent VEMP response. Latencies of the n10 peak were averaged between the two sides for subjects with bilateral oVEMP responses (correlation coefficient 0.66, $p<0.0001$). The peak-to-peak amplitude was calculated as the sum of the n10 and p16 amplitudes. Asymmetry ratio (AR) between a subject's ears was calculated according to the formula:

$$AR = \left| \frac{\text{Left\_amplitude} - \text{Right\_amplitude}}{\text{Left\_amplitude} + \text{Right\_amplitude}} \right| \times 100\%$$

The cVEMP waveform consists of a positive peak (p13), identified as the first distinctive trough in the waveform, followed by a negative peak (n23), identified as the first distinctive peak in the waveform. Background EMG activity was recorded during the 10-ms interval before stimulus onset. Subjects with EMG recordings lacking definable p13 waves were

defined as having an absent VEMP response. Latencies of the p13 peak were averaged between the two sides for subjects with bilateral cVEMP responses (correlation coefficient 0.46, $p<0.0001$). The raw peak-to-peak amplitude was calculated as the sum of the p13 and n23 amplitudes and rectified amplitude was calculated by the raw peak-to-peak amplitudy by the background activity. Asymmetry ratio (AR) was calculated using the above formula.

Analysis

For subjects exhibiting VEMP responses, either unilaterally or bilaterally, parameters including latency, amplitude, and asymmetry ratio, were evaluated and then stratified by demographic and cardiovascular risk categories. Analysis of variance (ANOVA) was used to evaluate whether VEMP latency, amplitude and asymmetry ratio differed significantly between age groups (<50 years, 50-59, 60-69, 70-79, and 80+ years). To include subjects with absent responses in our analyses, we categorized VEMP responses into two groups: individuals with any VEMP loss (i.e. bilateral or unilateral absence of VEMP response) and individuals with bilaterally present VEMP responses. Multiple linear regression was used to analyze continuous outcome measures, in which β refers to the slope of the linear regression, and multiple logistic regression was used for categorical outcomes. All analyses were carried out in Stata Data Analysis and Statistical software (College Station, TX, USA). $P < 0.05$ was considered statistically significant.

Results

Ocular VEMP Results

Two hundred fifty-seven subjects with mean age 72.9 years (standard deviation, 12.6; range, 26 - 92 years) underwent oVEMP testing (Table 1). Six percent of subjects were under 50 years of age, 6% were age 50-59, 27% were age 60-69, 27% were age 70-79, and 34% were age 80 and older. Male subjects comprised 43% of the study sample. Sixty-six percent of the subjects were white and 25% of the subjects were black. Of the remaining 9%, only five subjects had a race of “other” and 15 subjects had unknown race, therefore only whites and blacks were included in the analysis. Forty-eight percent of the subjects reported a positive history of hypertension, 17% of the subjects reported a positive history of diabetes mellitus, and 69% of the subjects reported a positive history of hyperlipidemia. Forty-two percent of the subjects reported a positive smoking history. Forty-four subjects (17%) exhibited bilateral loss of oVEMPs and 9 (3%) subjects exhibited unilateral loss of oVEMPs.

We evaluated for differences in oVEMP latency, amplitude and asymmetry ratio by demographic and cardiovascular characteristics in the 213 subjects who displayed at least one oVEMP response. ANOVA analyses revealed significant differences in n10 latency and peak-to-peak amplitude across age categories ($p = 0.010$ and $p < 0.0001$, respectively) (Table 1). N10 latencies increased with increasing age category, and peak-to-peak amplitudes decreased with increasing age category. No significant differences were found for n10 latency or peak-to-peak amplitude between males and females. We observed in bivariate analyses that n10 latency is significantly longer in white participants compared to black participants, while peak-to-peak amplitude is significantly smaller in white participants compared to black participants ($p = 0.0003$ and $p < 0.0001$, respectively). We

did not observe any significant differences in oVEMP amplitudes or latencies across cardiovascular risk groups. Additionally, asymmetry ratio did not differ significantly across any demographic or cardiovascular risk groups.

In multiple linear regression models including age (as a continuous variable), sex, race, hypertension, diabetes mellitus, hyperlipidemia and smoking status, we observed that oVEMP n10 latency increased with age (0.12 ms/decade, $p = 0.002$) while peak-to-peak amplitude decreased with age (2.9 μV/decade, $p < 0.001$) (Table 2). In multivariate analyses, black participants had a significantly shorter oVEMP n10 latency ($\beta = -0.270$, $p = 0.013$) and an increased peak-to-peak amplitude ($\beta = 4.346$, $p = 0.002$) (Table 2). We plotted oVEMP latency and amplitude by age stratified by race (Figure 1). We observed that oVEMP latencies were shorter and oVEMP amplitudes were higher in black participants throughout the age range. However, interaction terms between age and race were not significant for n10 latency or peak-to-peak amplitude, suggesting that the slopes of decline of oVEMP function with age did not differ by race. No significant associations were found between asymmetry ratio and any of the demographic or cardiovascular risk characteristics in multivariate analyses.

We further created dichotomous categories of oVEMP loss and evaluated the odds of having any oVEMP loss (*i.e.*, unilateral or bilateral oVEMP loss) in multivariate analyses. We focused on differences by age categories, and in separate analyses we examined differences by combined sex and race categories (Tables 3 and 4). We combined individuals < 70 years old to create a single reference group of comparable size to the other two age groups (70-79 years, and ≥ 80 years). Twelve (13%) subjects < 70 years old exhibited any type of oVEMP loss compared to 12 (18%) subjects age 70-79 and 29 (29%) subjects age 80 and older. Subjects ≥ 80 years old had a 2.5-fold increased odds of any type of oVEMP loss relative to those age < 70 in multivariate models (OR 2.45, 95% CI: 1.01-5.90).

In multivariate analyses considering sex and race with white females as the reference group, black females had an 80% decreased odds of any oVEMP loss compared to white females (Prevalence 5% vs. 24%, odds ratio (OR) 0.21, 95% CI: 0.05-0.96). Out of 14 black males in this study population, none exhibited any type of oVEMP loss. For this reason, it was not possible to calculate an odds ratio for oVEMP loss in black males. Fisher's exact test showed a significant difference in proportions of any oVEMP loss among white females (24.4%), white males (28.7%), black females (5.0%), and black males (0%) ($p = 0.002$).

Cervical VEMP Results

Two hundred fifty subjects with mean age 72.6 years (standard deviation, 12.5; range, 26 - 92 years) underwent cVEMP testing (Table 5). Seven percent of subjects were under 50 years of age, 8% were age 50-59, 28% were age 60-69, 27% were age 70-79, and 31% were age 80 and older. Male subjects comprised 46% of subjects. Sixty-eight percent of the subjects were white and 24% of the subjects were black. Forty-seven percent of the subjects reported a positive history of hypertension, 17% of the subjects reported a positive history of diabetes mellitus, and 68% of the subjects reported a positive history of hyperlipidemia. Forty-two percent of the subjects reported a positive smoking history. Six subjects underwent cVEMP testing on only one side due to technical difficulties or ineligibility on

the opposite side and were excluded from the categorical analyses examining cVEMP loss. Out of those six subjects, two exhibited cVEMP loss on the tested side. Out of 244 subjects who underwent bilateral cVEMP testing, 64 (26%) subjects exhibited bilateral loss of cVEMPs and 54 (22%) subjects exhibited unilateral loss of cVEMPs. Subjects were significantly more likely to experience bilateral loss of air-conducted cVEMP compared to midline tap oVEMP (26% *vs*. 17%, p = 0.015).

We evaluated for differences in cVEMP latency, amplitude and asymmetry ratio by demographic and cardiovascular characteristics in 184 subjects (180 subjects who exhibited at least one response during bilateral testing and four subjects who exhibited a response during unilateral testing). There was no significant difference in p13 latency across age or ethnicity groups, although p13 latency was significantly longer in males (p = 0.005) (Table 5). P13 latency did not differ significantly across any cardiovascular risk factor groups. ANOVA analyses revealed significant differences in corrected cVEMP amplitude across age categories (p = 0.014). Corrected amplitude decreased with increasing age categories. There was no significant difference in corrected cVEMP amplitude across ethnicity groups or between males and females. We observed that corrected cVEMP amplitude was lower in hypertensives (p = 0.020). Asymmetry ratio did not differ significantly across any demographic or cardiovascular risk factors.

In multiple linear regression models adjusting for age (as a continuous variable), sex, race, hypertension, diabetes mellitus, hyperlipidemia and smoking status, we observed that corrected cVEMP amplitude decreased with age (0.14/decade, p = 0.005) (Table 6). We found that cVEMP p13 latency is longer in males (β = 0.381, p = 0.021), and we observed a trend towards higher corrected amplitudes in males (β = 0.232, p = 0.055). No significant differences were found for p13 latency or corrected amplitude between white and blacks. We plotted cVEMP latency and amplitude by age as a function of sex (Figure 2). Interaction terms between age, race, and sex were not significant for p13 latency or corrected amplitude, suggesting no difference in slopes of decline associated with age. The relationship between cVEMP amplitude and history of hypertension was not significant in multivariate analysis. No significant associations were found between asymmetry ratio and any demographic or cardiovascular risk characteristics.

Similar to the oVEMP analysis, we created dichotomous categories of cVEMP loss and evaluated the odds of having any cVEMP loss (*i.e.*, unilateral or bilateral cVEMP loss), according to demographic and cardiovascular characteristics (Tables 7 and 8). We combined individuals < 70 years old to create a single reference group of comparable size to the other two age groups (70-79 years, and ≥ 80 years). Twenty-six (29%) subjects < 70 years old exhibited any type of cVEMP loss compared to 28 (45%) subjects age 70-79 and 64 (69%) subjects age 80 and older. Subjects age 70-79 years had a 4-fold increased odds of any type of cVEMP loss relative to those age < 70 in adjusted models (OR 4.02, 95% CI: 1.80-8.99). Subjects age 80 years and older had a 7-fold increased odds of any type of cVEMP loss relative to those age < 70 in adjusted models (OR 7.02, 95% CI: 3.23-15.27).

In adjusted analyses, white males had a 60% decreased odds of any cVEMP loss compared to white females (Prevalence 45% vs. 60%, OR 0.41, 95% CI: 0.20-0.86). Similarly, black

females had a 65% decreased odds of any cVEMP loss compared to white females (Prevalence 26% vs.60%, OR 0.36, 95% CI: 0.14-0.90).

Discussion

This study in healthy community-dwelling adults corroborates previous reports of declines in otolith function associated with age. Specifically, we found that oVEMP n10 latency increased while peak-to-peak amplitude decreased with age. Similarly, corrected cVEMP amplitude decreased with age. For both oVEMPs and cVEMPs, the odds of absent VEMP responses were significantly higher in older age groups. These data support previous epidemiologic and pathologic findings that otolith dysfunction increases with age (Piker et al., Johnsson et al., 1972, Igarashi et al., 1993, Rauch et al., 2001, Welgampola et al., 2001, Zapala et al., 2004, Brantberg et al., 2007, Walther et al., 2007, Janky et al., 2009, Rosengren et al., 2011, Agrawal et al., 2012, Kantner et al., 2012, Taylor et al., 2012, Singh et al., 2013). Using click, tone burst, and midline tap stimuli, Nguyen et al. showed that subjects > 50 years old were found to have significantly decreased oVEMP and cVEMP amplitudes (Nguyen et al. 2010) while no age effects were found for latencies or asymmetry ratios. Janky et al. used tone burst stimuli of various frequencies and found that significant differences in cVEMP threshold for 500 and 700 Hz tone bursts exist between age groups, with lower thresholds in younger age groups. Interestingly, cVEMP p13 latency for 250, 750, and 1000 Hz toneburst stimuli was found to be longer in younger age groups (Janky et al., 2009).

A novel finding of this study is the significant difference in oVEMP latency and amplitude by race. In unadjusted and adjusted analyses, black participants had significantly better oVEMP function, as evidenced by shorter oVEMP n10 latency, increased peak-to-peak amplitude, and decreased odds of absent oVEMP responses. One potential mechanism to explain these findings relates to melanin pigmentation. Melanin appears to be present at concordant levels in the skin and labyrinth (Wolff, 1931), such that dark-skinned individuals have more melanin in their labyrinthine neuroepithelia. Melanin may protect against age-related loss of labyrinthine function. Ultrastructural studies of the human labyrinth have demonstrated the presence of melanocytes in the vestibular organs, particularly in the semicircular canals and utricle (Masuda et al., 1995). Experiments performed in guinea pigs suggest that melanin regulates the ionic composition of the endolymphatic fluids (Meyer zum Gottesberge-Orsulakova, 1985). Other human pathologic analyses report melanocytes in close spatial arrangement with vestibular dark cells, suggesting that melanocytes may take part in vestibular organ metabolism via the dark cells and neighboring capillaries (Igarashi et al., 1989). Darks cells exist in all vestibular organs except the saccular macula, which may explain why racial differences were observed solely in oVEMPs, reflecting utricular function, rather than cVEMPs, reflecting saccular function (Goldberg et al., 2012). Other potential mechanisms to explain the observed race-based differences in oVEMP include genetic as well as environmental differences. In a similar vein, several recent studies observed an association between greater skin pigmentation and lower levels of hearing loss (Lin et al., 2011, Sun et al., 2014). Ongoing investigations are evaluating whether better otolith function in blacks may contribute to the lower fall and hip fracture rates observed in blacks.

We also observed prolonged p13 latencies in males, consistent with a previous study that evaluated cVEMPs evoked by 500 Hz tone bursts (Brantberg et al., 2007). Similar to previous studies (Brantberg et al., 2001, Rosengren et al., 2011), we did not observe a significant association between sex and corrected cVEMP amplitude, although there was a trend towards higher amplitudes in males. We did not observe any significant sex-related differences in oVEMP latencies or amplitudes, consistent with some (Rosengren et al., 2011) though not all studies (Sung et al., 2010). Sex-related anatomic differences in the otolith organ have been reported in the literature. Three-dimensional measurements of the human vestibular apparatus have shown that males tend to have larger surface areas of the utricular and saccular maculae (Sato et al., 1992). However, these anatomic differences have not been directly correlated with VEMP testing results, and whether they contribute to the cVEMP latency prolongation observed in males in this study is unclear. Increased head size in males may play a role in longer latencies. Although no study directly evaluated head size and VEMP latencies, several studies have shown significant positive correlations between head diameter and auditory brainstem response (ABR) latencies (Trune et al., 1988, Nikiforidis et al., 1993). Similarly, for a given head size, women have been found to have lower neck cross-sectional area and muscle mass compared to men (Vasavada et al., 2008). Additionally, individuals with longer necks have been shown have later cVEMP responses because the efferent signal has to travel a longer distance (Chang et al., 2007). These geometrical differences between males and females may also contribute to longer cVEMP latencies in males.

Although previous adjusted analyses from NHANES demonstrated a significantly higher prevalence of vestibular dysfunction associated with diabetes mellitus (Agrawal et al., 2009), in our study population, cardiovascular risk factors had no significant association with VEMP latency, amplitude or asymmetry ratio in multiple linear regression analyses. These findings are consistent with other clinical investigations showing no significant difference in cVEMP responses between non-insulin-dependent diabetics and healthy individuals (Bektas et al., 2008). Although cardiovascular risk factors were not correlated with chances in VEMP parameters in adjusted analyses, corrected cVEMP amplitude was found to be lower in individuals with hypertension. This result is concordant with findings from NHANES showing a significant difference in the prevalence of vestibular dysfunction between individuals with and without a history of hypertension. After adjusting for age, race, sex, educational level, smoking status, and diabetes, a history of hypertension was associated with a borderline significant increase in the odds of vestibular dysfunction ($p = 0.06$) (Agrawal et al., 2009). Discrepancies between the present study and the NHANES study may be attributed to the fact that cardiovascular risk factors may play a greater role in global measures of balance function (used in NHANES) vs. the more specific measures of otolith function used in this study. Moreover, participants in the BLSA appear to be healthier and have less burden of cardiovascular disease compared to participants in NHANES. For example, while 25.4% of the NHANES study population reported a ≥ 20 pack-year smoking history, our study population averaged 3.2 pack-years, with a maximum reported smoking history of 9 pack-years.

We observed that bilateral response loss occurred more frequently with cVEMP testing compared to oVEMP testing, which may suggest that the prevalence of saccular dysfunction

is higher in older adults compared to utricular dysfunction. This finding supports a previous study that demonstrated differential vestibular decline associated with aging, with greater age-related losses occurring in saccular relative to utricular function (Agrawal et al., 2012). Furthermore, these findings are consistent with histopathological evidence that reports greater degrees of age-related hair cell loss in the saccular compared to utricular macula (Rauch et al., 2001, Walther et al., 2007), and greater age-related degradation of otoconia in the saccule relative to the utricle (Johnsson et al., 1972, Igarashi et al., 1993). Alternatively, the relative sparing of utricular function may reflect the differential test sensitivity of the midline tap oVEMP and sound-evoked cVEMP. The tap-evoked oVEMP test has been shown to deliver a suprathreshold stimulus and thus may not be as sensitive to losses in utricular function (Halmagyi et al., 1995) compared to the sound-evoked cVEMP, which relies on a less intense, non-physiologic stimulus.

Several limitations of this study should be noted. Because this was a cross-sectional study, causal inferences cannot be made. Further longitudinal studies from the BLSA population are in progress and will address this limitation. Additionally, participants in the BLSA are subject to a strict screening process and represent a population of healthy, well-functioning adults compared to the US population. Therefore, findings may not be applicable to a population presenting to clinics with balance complaints. Potential methodological limitations of VEMP testing should also be considered. Because otolith function is evaluated based on an oligosynaptic reflex involving the inferior oblique or sternocleidomastoid muscles, VEMP testing results in our older population may be biased due to impaired function of the efferent limb of the reflex. Studies differ regarding the presence and extent of age-related degradation in efferent motor function (Basta et al., 2007, Akin et al., 2011).

In this study, we confirm the presence of age-related declines in otolith function and report significantly better oVEMP function in blacks relative to whites across the age range. Further studies are in progress to establish the clinical and functional correlates of these age, sex- and race-based differences in VEMP results.

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Highlights

- Black race was associated with better oVEMP function (shorter n10 latency and greater peak-to-peak amplitude) across the age range.
- Ocular VEMP latency and amplitude, along with cervical VEMP corrected amplitude, exhibit age-related declines.
- Cardiovascular risk factors, including hypertension, diabetes mellitus, hyperlipidemia, and smoking history, had no associations with VEMP latency, amplitude or asymmetry ratio.

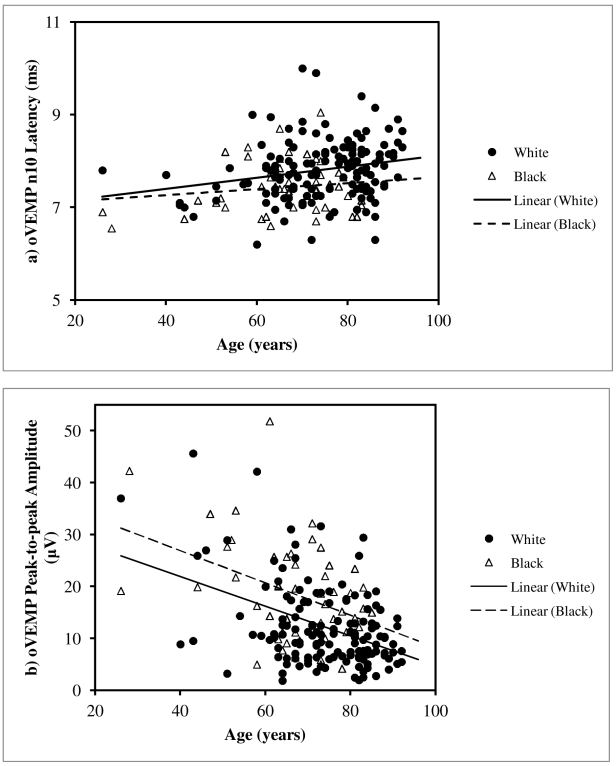

Figure 1.

Ocular VEMP n10 latency (a) and peak-to-peak amplitude (b) by age and race in the Baltimore Longitudinal Study of Aging

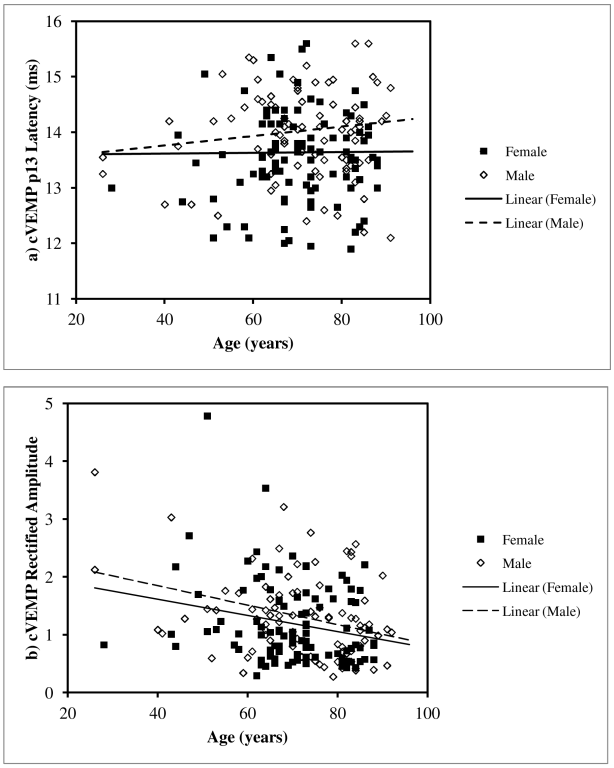

Figure 2.

Cervical VEMP p13 latency (a) and corrected amplitude (b) by age and sex in the Baltimore Longitudinal Study of Aging

Table 1

Ocular VEMP latency, amplitude and asymmetry ratio stratified by demographic and cardiovascular risk characteristics in the Baltimore Longitudinal Study of Aging.

Demographic Characteristics	No. (%) of Participants	oVEMP n10 Latency (SD)	P Value	oVEMP Peak-to-peak Amplitude (SD)	P Value	oVEMP Asymmetry Ratio (SD)	P Value
All participants[a]	257	7.70 (0.64)	---	13.86 (8.87)	---	17.3 (13.3)	---
Bilateral oVEMP loss	44 (17.1)						
Unilateral oVEMP loss	9 (3.5)						
Age							
<50 years	12 (5.6)	7.09 (0.36)	0.010	24.83 (12.95)	<0.0001	0.19 (0.17)	0.552
50-59	12 (5.6)	7.70 (0.60)		20.37 (12.26)		0.17 (0.18)	
60-69	58 (27.2)	7.67 (0.57)		15.00 (9.01)		0.15 (0.14)	
70-79	58 (27.2)	7.78 (0.71)		12.80 (7.06)		0.17 (0.12)	
80+	73 (34.3)	7.77 (0.63)		10.91 (6.41)		0.19 (0.12)	
Sex							
Male	92 (43.2)	7.77 (0.62)	0.216	13.19 (8.67)	0.337	0.17 (0.14)	0.862
Female	121 (56.8)	7.66 (0.65)		14.37 (9.01)		0.18 (0.13)	
Race/ethnicity[b]							
White	140 (65.7)	7.80 (0.64)	0.0003	12.24 (7.96)	<0.0001	0.19 (0.14)	0.088
Black	53 (24.9)	7.44 (0.56)		18.5 (9.63)		0.15 (0.11)	
Other	5 (2.3)	8.01 (0.39)		10.65 (4.49)		0.20 (0.12)	
Unknown	15 (7.1)	7.63 (0.67)		13.60 (10.00)		0.14 (0.10)	
Cardiovascular Risk Factors							
Hypertension							
Yes	99 (47.6)	7.64 (0.62)	0.140	13.50 (7.41)	0.506	0.18 (0.12)	0.449
No	109 (52.4)	7.78 (0.65)		14.3 (10.08)		0.17 (0.15)	
Diabetes Mellitus							
Yes	35 (16.9)	7.70 (0.65)	0.619	13.82 (8.97)	0.635	0.18 (0.13)	0.644
No	172 (83.1)	7.76 (0.59		14.61 (8.75)		0.16 (0.14)	
Hyperlipidemia							
Yes	143 (69.1)	7.69 (0.66)	0.770	13.17 (7.82)	0.452	0.18 (0.15)	0.978
No	64 (30.9)	7.72 (0.63)		14.2 (9.29)		0.17 (0.13)	
Smoking History							
Yes	87 (42.2)	7.74 (0.67)	0.529	14.20 (9.37)	0.599	0.17 (0.13)	0.495
No	119 (57.8)	7.68 (0.60)		13.53 (8.33)		0.18 (0.14)	

[a] Two subjects underwent oVEMP testing on one side only.

[b] Only five subjects had a race of “other” or “unknown”, therefore only whites and blacks were included in the analysis.

Table 2

Multiple linear regression analysis of oVEMP latency, amplitude and asymmetry ratio with demographic and cardiovascular risk factors. Significant factors are indicated with an asterisk.

Characteristics	oVEMP n10 Latency		oVEMP Peak-to-peak Amplitude		oVEMP Asymmetry Ratio	
	$r^2 = 0.13$		$r^2 = 0.26$		$r^2 = 0.03$	
	β	P value	β	P value	β	P value
Age	0.012	0.002*	−0.291	<0.001*	0.000	0.685
Sex	0.080	0.400	0.557	0.645	−0.004	0.848
Race	−0.270	0.013*	4.346	0.002*	−0.045	0.071
Hypertension	−0.145	0.144	−0.057	0.964	0.021	0.360
Diabetes Mellitus	0.131	0.327	0.258	0.880	0.004	0.905
Hyperlipidemia	−0.020	0.841	1.116	0.383	−0.002	0.914
Smoking History	−0.094	0.310	−0.181	0.878	0.016	0.448

Table 3

Odds ratios of oVEMP loss by age adjusted for sex, race, hypertension, diabetes, hyperlipidemia, and smoking history

Age Group	Any oVEMP Loss	
	Prevalence (%)	OR (95% CI)
<70	12 (13.3)	1.00
70-79	12 (18.2)	1.83 (0.67-4.97)
80+	29 (29.3)	2.45 (1.01-5.90)

Table 4

Odds ratios of oVEMP loss by sex and race adjusted for age, hypertension, diabetes, hyperlipidemia, and smoking history

Race	Any oVEMP Loss	
	Prevalence (%)	OR (95% CI)
Caucasian Female	22 (24.4)	1.00
Caucasian Male	25 (28.7)	1.22 (0.59-2.53)
African American Female	2 (5.0)	0.21 (0.05-0.96)
African American Male	0 (0.0)	-

Table 5

Cervical VEMP latency, amplitude and asymmetry ratio stratified by demographic and cardiovascular risk characteristics in the Baltimore Longitudinal Study of Aging.

Demographic Characteristics	No. (%) of Participants	cVEMP p13 Latency (SD)	P Value	cVEMP Rectified Amplitude (SD)	P Value	cVEMP Asymmetry Ratio (SD)	P Value
All participants[a]	250	13.8 (0.95)	---	1.25 (0.72)	---	0.27 (0.20)	---
Bilateral cVEMP loss	64 (26.2)						
Unilateral cVEMP loss	54 (22.1)						
Age			0.713		0.014		0.451
<50 years	13 (7.0)	13.71 (1.04)		1.80 (0.98)		0.29 (0.17)	
50-59	14 (7.5)	13.49 (1.17)		1.42 (1.06)		0.21 (0.14)	
60-69	52 (28.0)	13.82 (0.77)		1.33 (0.71)		0.28 (0.21)	
70-79	50 (26.9)	13.87 (0.94)		1.21 (0.60)		0.31 (0.21)	
80+	57 (30.6)	13.86 (1.03)		1.06 (0.61)		0.24 (0.19)	
Sex			0.005		0.257		0.802
Male	85 (45.7)	14.03 (0.88)		1.32 (0.72)		0.27 (0.19)	
Female	101 (54.3)	13.64 (0.97)		1.20 (0.73)		0.29 (0.21)	
Race/ethnicity[b]			0.835		0.105		0.066
Caucasian	126 (67.7)	13.81 (0.93)		1.19 (0.67)		0.30 (0.20)	
African American	45 (24.1)	13.85 (1.04)		1.39 (0.87)		0.23 (0.17)	
Other	5 (2.7)	13.30 (1.01)		1.35 (0.63)		0.36 (0.32)	
Unknown	10 (5.4)	13.91 (0.68)		1.35 (0.73)		0.06 (0.05)	
Cardiovascular Risk Factors	**No. (%) of Participants**	**cVEMP p13 Latency (SD)**	**P Value**	**cVEMP Rectified Amplitude (SD)**	**P Value**	**cVEMP Asymmetry Ratio (SD)**	**P Value**
Hypertension			0.282		0.020		0.185
Yes	86 (47.0)	13.74 (0.92)		1.12 (0.61)		0.25 (0.20)	
No	97 (53.0)	13.89 (0.98)		1.37 (0.80)		0.30 (0.20)	
Diabetes Mellitus			0.850		0.974		0.688
Yes	31 (17.0)	13.84 (0.88)		1.25 (0.62)		0.26 (0.19)	
No	151 (83.0)	13.91 (0.97)		1.25 (0.75)		0.28 (0.20)	
Hyperlipidemia			0.664		0.267		0.991
Yes	124 (68.1)	13.84 (0.96)		1.21 (0.72)		0.28 (0.20)	
No	58 (31.9)	13.77 (0.94)		1.34 (0.74)		0.28 (0.18)	
Smoking History			0.714		0.246		0.934
Yes	75 (41.7)	13.84 (0.99)		1.32 (0.69)		0.28 (0.20)	
No	105 (58.3)	13.79 (0.93)		1.20 (0.75)		0.28 (0.20)	

[a] Six subjects underwent cVEMP testing on one side only.

[b] Only five subjects were neither black nor white, therefore only white and blacks were included in the analysis.

Table 6

Multiple linear regression analysis of cVEMP latency, EMG-corrected amplitude and asymmetry ratio with demographic and cardiovascular risk factors. Significant factors are indicated with an asterisk.

Characteristics	cVEMP p13 Latency		cVEMP Rectified Amplitude		cVEMP Asymmetry Ratio	
	$r^2 = 0.06$		$r^2 = 0.12$		$r^2 = 0.04$	
	β	P value	β	P value	β	P value
Age	0.010	0.125	−0.014	0.005*	0	0.846
Sex	0.381	0.021*	0.232	0.055	−0.004	0.917
Race	0.261	0.167	0.129	0.353	−0.057	0.214
Hypertension	−0.217	0.186	−0.157	0.194	−0.039	0.356
Diabetes Mellitus	−0.006	0.979	−0.101	0.529	−0.016	0.774
Hyperlipidemia	0.054	0.750	−0.096	0.440	0.024	0.583
Smoking History	0.016	0.917	0.149	0.199	0.02	0.615

Table 7

Odds ratios of cVEMP loss by age adjusted for sex, race, hypertension, diabetes, hyperlipidemia, and smoking history

Age Group	Any cVEMP Loss	
	Prevalence (%)	OR (95% CI)
<70	26 (29.2)	1.00
70-79	28 (45.2)	4.02 (1.80-8.99)
80+	64 (68.8)	7.02 (3.23-15.27)

Table 8

Odds ratios of cVEMP loss by sex and race adjusted for race, hypertension, diabetes, hyperlipidemia, and smoking history

Race	Any cVEMP Loss	
	Prevalence (%)	OR (95% CI)
White Female	53 (59.6)	1.00
White Male	36 (45.0)	0.41 (0.20-0.86)
Black Female	10 (26.3)	0.36 (0.14-0.90)
Black Male	4 (28.6)	0.43 (0.11-1.68)