Relationship Between Corrective Saccades and Measures of Physical Function in Unilateral and Bilateral Vestibular Loss

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Objectives: Following the loss of vestibular function, some patients functionally improve and are minimally bothered by their loss of peripheral function while others remain more symptomatic and are unable to return to their activities of daily living. To date, the mechanisms for functional improvement remain poorly understood. The purpose of the present study was to examine the association between corrective saccades and measures of handicap, dynamic visual acuity, gait, and falls.

Design: A retrospective chart review was performed to identify patients who were diagnosed with unilateral or bilateral vestibular hypofunction and who also completed a baseline vestibular rehabilitation evaluation. A total of 82 patients with unilateral vestibular hypofunction and 17 patients with bilateral vestibular hypofunction were identified. The video head impulse test results for each patient were grouped based on the type of presenting saccades. Specifically, the saccade grouping included the following: (1) covert, (2) overt, or (3) a combination of both types of saccades.

Results: The results show that covert saccades are associated with better performance on measures of dynamic visual acuity, gait, and balance in patients with unilateral vestibular hypofunction. Patients exhibiting overt saccades or combination of both covert and overt saccades were more often found to have an abnormal gait speed and be characterized as being at risk for falls using the Dynamic Gait Index. We observed no differences in physical function for those patients with bilateral vestibular hypofunction as a function of saccade grouping.

Conclusions: When comparing saccade groups (covert, overt, or combination of both), patients with unilateral vestibular hypofunction and covert saccades demonstrated better performance on standard baseline physical therapy measures of dynamic visual acuity and gait and balance. We did not observe any significant associations between saccade group and physical function in patients with bilateral vestibular hypofunction; however, additional studies are needed with adequate sample sizes. Our findings may suggest that corrective saccade latency in patients with unilateral vestibular hypofunction is related to measures of physical function. The extent to which saccade latency has the potential to be a useful target for vestibular rehabilitation is still to be determined and may be promising target to improve functional outcomes.

Key words: Balance, Bilateral vestibular hypofunction, corrective saccades, Dizziness handicap, Dynamic Gait Index, Dynamic visual acuity, Falls, Gain, Physical function, Unilateral vestibular hypofunction, Vestibular, Video head impulse test.

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INTRODUCTION

The vestibular ocular reflex (VOR) ensures gaze stability during head rotation by generating eye movements that are equal and opposite to head rotation. When vestibular loss is present, an individual is unable to maintain gaze on a target during ipsilesional head rotation. Instead, the eyes move with the head (due to the reduction in VOR gain), which causes visual blurring for the patient with uncompensated vestibular loss. Clinically, we can identify a VOR deficit at bedside by completing a head impulse test. During this test, a patient is asked to maintain gaze on a target while the patient’s head is rapidly rotated left or right. In the case of the deficient VOR, the eyes move off target so that the patient must make a corrective eye movement (i.e., a corrective saccade) back to the target. These corrective saccades are considered to be diagnostic indicators of peripheral vestibular hypofunction (Halmagyi & Curthoys 1988; Halmagyi et al. 1990). More recently an instrumented version of the head impulse test (i.e., the video head impulse test [vHIT]) was developed. The vHIT allows for recording head and eyes movements in a busy clinical setting and allows for computerized analysis of the VOR. With these recordings, we now know that in addition to the saccades that can be detected by the clinician following a head impulse (i.e., overt saccades), there are also saccades which occur during the head impulse (i.e., covert saccades) that were previously undetected during head impulse testing (Bartl et al. 2009; MacDougall et al. 2009; Blodow et al. 2013). Moreover, recent evidence demonstrates that the latency and type of saccades differ for any given patient with vestibular hypofunction—that is, some patients may exhibit all overt saccades, all covert saccades or a combination of both overt and covert saccades (Weber et al. 2008; Schubert et al. 2010; Blodow et al. 2013; Mantokoudis et al. 2014; Batuecas-Caletrio et al. 2017).

While the presence of corrective saccades has long been viewed as a diagnostic indicator of peripheral vestibular loss in a clinical setting, eye movements such as saccades may also be considered an indicator of a compensatory mechanism to overcome the loss of peripheral vestibular function (Berthoz 1988; Black et al. 2005; Schubert & Zee 2010; Macdougall & Curthoys 2012). Specifically, saccades may be used to augment the diminished slow-phase component of the deficient VOR (Berthoz 1988; Schubert & Zee 2010) and therefore, may also offer insight into the status of central compensation mechanisms following vestibular loss. Researchers have begun to examine the functional effect of saccades. The prevalence, gain, and frequency of covert saccades (as opposed to overt saccades) were positively correlated with dynamic visual acuity performance (Wettstein et al. 2016; Hermann et al. 2017) in patients with unilateral (UVH) and bilateral vestibular hypofunction (BVH),
such that covert saccades were related to better dynamic visual acuity. Following acoustic neuroma resection, perceived dizziness handicap was correlated with the pattern of the saccades (Batuecas-Caletrio et al. 2014). Those whom had latency patterns that were organized (i.e., occurred at similar time points impulse to impulse) reported less symptoms than those who had variability in the saccade latency impulse to impulse (Batuecas-Caletrio et al. 2014, Batuecas-Caletrio et al. 2017). In five patients who underwent superior canal plugging for treatment of superior canal dehiscence, the authors noted during the initial post-operative period that saccade latencies reduced (i.e., overt saccades transitioned to covert saccades) for most patients over time; however, it is unclear the extent to which these changes were associated with symptom improvement as this was not reported (Mantokoudis et al. 2016). No data to date has examined the associations between saccadic parameters and measures of balance and gait in a patient population with vestibular hypofunction. The purpose of this study was to examine the associations between the timing of corrective saccades and measures of gait, balance, dynamic visual acuity, and self-reported symptoms in patients with vestibular hypofunction.

MATERIALS AND METHODS

This study was conducted as a retrospective analysis of vestibular laboratory test results and vestibular rehabilitation baseline measures that were routinely obtained within the Otolaryngology clinic at Duke University Medical Center. This study was approved by the local Institutional Review Board (Protocol: Pro00100329).

Participants

A retrospective chart review of patients was performed from January 2014 to June 2018. Individuals were eligible for inclusion in the present study if they were between the ages of 18–89 years of age, presented to the otolaryngology clinic with the chief complaint of dizziness and/or vertigo, and were seen for evaluation by the vestibular laboratory clinic, vestibular physical therapy, and otolaryngology within 15 days of each other (i.e., all measures of interest were collected within a 15-day window). We excluded individuals who demonstrated (1) an abnormal ocular motor exam in the vestibular laboratory, (2) individuals with legal blindness and/or vision reduced to the extent that ocular motor testing could not be carried out within the vestibular laboratory due to the inability to see the visual calibration target, (3) patients with known peripheral neuropathy, (4) patients with known neurodegenerative disease that may effect gait (e.g., Parkinson’s Disease), and (5) those with known orthopedic injury or lower limb amputation. While the presence of spontaneous nystagmus was not used as part of an exclusionary criteria, no participant showed evidence for spontaneous nystagmus.

Individuals were initially categorized into two groups based on vestibular laboratory test findings: (1) UVH or (2) BVH. Individuals were categorized as UVH if they demonstrated a unilateral vestibular weakness of 25% or greater during bilateral warm water caloric irrigations. Individuals were categorized as BVH if they demonstrated evidence of bilateral impairment during sinusoidal harmonic acceleration using a similar classification scheme as Judge et al. (2017). Specifically, sinusoidal harmonic acceleration gain at both 0.01 Hz and 0.08 Hz needed to be reduced with the presence of phase leads. In our clinic, gain is considered to be abnormally reduced if the gain is less than 0.15 at 0.01 Hz and less than 0.33 at 0.08 Hz. Abnormal phase leads are defined by phase leads greater than 52 at 0.01 Hz and greater than 12 at 0.08 Hz. In instances where gain was severely reduced (gains less than 0.15) phase was unreliable and in those cases, gain values only were used.

Vestibular Laboratory Measures of Interest

Video Head Impulse Test • Results from the vHIT were extracted from the medical record and data collection device. vHIT was administered by a trained clinician using the Interacoustics EyeSeeCam (Interacoustics USA, Eden Prairie, MN, USA). During testing, individuals were asked to focus on a target at a distance of 1 m. The video goggle cameras were calibrated using the manufacturer’s recommended calibration routine. The examiner stood behind the individual and placed their hands on the lower jaw and mandible. Horizontal head impulses (10–20° displacement; 150–300°/s peak head velocity) were applied and were random in onset presentation and direction. A minimum of 10 impulses up to a maximum of 20 impulses per impulse direction were obtained. Outcome measures of interest were gain (defined by instantaneous velocity gain at 60 ms) and saccade latency. Based on our clinical normative data, a vHIT result was considered normal if the VOR gain was ≥0.80 regardless of the presence or absence of saccades. A vHIT result was considered abnormal when the gain was reduced (<0.80) and there were either covert or overt saccades present. Individual files were analyzed in MATLAB (version, 9.5). Data were first analyzed for artifact according to Mantokoudis classification scheme and artifacts were removed (Mantokoudis et al. 2015). Next individual vHIT slow-phase velocity waveforms were manually analyzed to identify vHIT waveform start time, vHIT waveform end time, peak head velocity, peak eye velocity, and the peak velocity and latency of each corrective saccade using custom Matlab software (Janky et al. 2018). To be considered a corrective saccade, the amplitude of the saccade needed to exceed 50°/s. These data were then exported and used for analysis. Head impulse saccade data for each individual were characterized as (1) predominantly covert (Covert), (2) predominantly overt (Overt), or (3) a combination of both covert and overt saccades (Combination). Predominantly covert (or overt) was defined as at least 80% of all impulses (in one direction for UVH and both directions for BVH) for an individual were covert (or overt). To be characterized as a combination of both types of saccades, the individual produced both covert and overt saccades and did not meet the threshold of 80% of impulses of either covert or overt saccades. We examined these saccade groups in both the UVH and BVH patients.

Physical Function Outcome Measures of Interest

Several measures were obtained from the initial vestibular rehabilitation evaluation to probe dynamic visual acuity, gait and balance performance, and falls history. All vestibular rehabilitation measures were performed by a physical therapist certified in vestibular rehabilitation.

Dizziness Handicap Inventory • The DHI is a 25-item self-report questionnaire that probes the perceived handicap of the patient due to dizziness and unsteadiness. The total score of the DHI was recorded for each patient. DHI scores range from 0

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to 100 with a higher score being consistent with more handicap (Jacobson & Newman 1990).

**Clinical Dynamic Visual Acuity** • The clinical dynamic visual acuity (cDV A) was performed using horizontal active head motion while using an Early Treatment Diabetic Retinopathy Study chart at 4 feet. Visual acuity is initially measured while the head is stationary (static visual acuity) and then visual acuity is measured while the individual turns his/her head left and right at a frequency of approximately 2 Hz (dynamic visual acuity). The number of lines of difference from static visual acuity and dynamic visual acuity were calculated and used for analysis. Fewer lines of difference indicate better dynamic visual acuity and a difference of three lines or more is considered abnormal.

**Preferred Gait Speed** • Patients were asked to walk at their preferred gait speed for a distance of 30 feet and the time to walk the middle 20 feet was recorded using a stopwatch. A gait speed of less than 1.0 m/s was used as the criteria for abnormal.

**Falls History** • Each patient was asked about falls in the past 6 months due to his/her dizziness. Data were dichotomized as either yes/no for a fall.

**Statistical Approach**

Descriptive statistics (means and SDs) were used to describe demographic variables for the patient cohorts based on the clinical diagnosis of UVH or BVH. A series of Chi-Square and Fisher’s exact test were used to evaluate the associations between categorical vestibular rehabilitation baseline measures and vHIT saccade group (Covert, Overt, Combination). Analyses of variance (ANOVA) tests were used to examine the effects of continuous vestibular rehabilitation baseline measures as a function of saccade group. Post-hoc testing using Bonferroni corrections were examined to determine group differences when the overall ANOVA was significant. The same statistical approach was used separately for UVH and BVH patients, and the results are presented separately for UVH and BVH groups. All statistical analyses were conducted using IBM SPSS Version 25 and significance was set at $p < 0.05$ for all analyses.

**RESULTS**

**Cohort Demographics and Patient Characteristics**

Among the patient population, 82 individuals were diagnosed with having UVH. The mean age of individuals with UVH was 54 years (SD = 16 years; range 26–88 years). There were 51 females and 31 males. Seventeen individuals were characterized as BVH. The mean age of individuals with BVH was 59 years (SD = 15 years; range 18–81 years). There were 6 females and 11 males.

**Unilateral Vestibular Hypofunction Physical Function Outcomes**

Of the 82 individuals who were characterized as having UVH, 75 had abnormal vHIT responses (i.e., gain less than 0.80 with the presence of saccades) and were included in the analysis. The other seven patients had normal vHIT results with abnormal caloric and were excluded. Of the 75 individuals included, 10 individuals were characterized as having predominantly covert saccades (Covert), 41 as overt saccades (Overt), and 24 as a combination of covert and overt (Combination) based on their vHIT saccade results. There was no difference in age among the three saccade groups (F(2, 74) = 0.381)

As seen in Figure 1 (panel A), the mean DHI score (and SD) were 48 (23), 47 (21), and 54 (21), for Covert, Overt, and Combination saccade groups, respectively. An ANOVA revealed no significant difference in mean DHI scores as a function of saccade group in the UVH patients (F(2,63) = 0.58, $p = 0.58$).

As seen in Figure 2 (panel A), the mean cDV A line loss (and SD) was 2.6 (1.4), 4.5 (2.1), and 4.9 (1.9) for Covert, Overt, and Combination groups, respectively. An ANOVA confirmed a significant difference in cDV A loss as a function of saccade group (F(2, 69) = 5.25, $p = 0.002$). Post-hoc analyses with Bonferroni corrections demonstrated lower (i.e., better) cDV A line loss in patients with Covert saccades compared to either Overt saccades ($p = 0.006$) or those with a Combination of saccades ($p = 0.002$).
The percent of patients with abnormal and normal responses for gait speed were calculated as a function of saccade group and are illustrated in Figure 3 (panel A). All patients in the Covert group demonstrated normal gait speed (≥1 m/s); whereas, 46% of the Overt group and 50% of the Combination group had abnormal gait speed. A significant difference between the proportion of individuals who had normal preferred gait speed between groups was observed (Fisher’s Exact = 9.2; \( p = 0.01 \)).

The mean 4-item DGI score (and SD) was 10.7 (1.2), 8.75 (1.7), 8.4 (2.4) for the Covert, Overt, and Combination groups, respectively. An ANOVA revealed that there was a significant difference in mean DGI score as a function of saccade group (F(2, 70) = 5.22, \( p = 0.008 \)). Post-hoc analyses with Bonferroni correction for multiple comparisons demonstrated higher (i.e., better) DGI scores in patients with Covert saccades compared to either Overt (\( p = 0.006 \)) or Combination saccades (\( p = 0.002 \)). Further, when looking at fall risk based on a cutoff score of ≤9 on the DGI (Fig. 4, panel A), there was a significant difference in the proportion of individuals who had scores that were consistent with increased falls risk (Fisher’s exact test = 6.1; \( p = 0.04 \)). Only 20% of Covert group showed evidence for increased falls risk; whereas, nearly 60% in the Overt and the Combination groups were at increased fall risk. Interestingly (Fig. 5, panel A) this did not translate to differences in self-reported falls as there were no significant differences among saccade groups (Fisher’s exact test = 0.211, \( p = 0.94 \)).

### Bilateral Vestibular Hypofunction

#### Physical Function Outcomes

Based on vHIT saccade results of the 17 individuals diagnosed with BVH, 4 individuals were characterized as Covert, 5 as Overt, and 8 as Combination saccades. There was no difference in age among the three saccade groups (F(2, 14) = 0.862).

The mean DHI score (and SD) for the Covert group was 6.5 (0.6), for Overt was 8.2 (1.0), and for the Combination was 6.1 (2.2) (Fig. 2, panel B). An ANOVA revealed no significant difference in mean DHI as a function of saccade group (F(2,12) = 0.49, \( p = 0.62 \)).

The mean DVA line loss (and SD) for the Covert group was 6.5 (0.6), for Overt was 8.2 (1.0), and for the Combination was 6.1 (2.2) (Fig. 2, panel B). An ANOVA revealed no significant difference in cDVA loss as a function of saccade group (F(2, 13) = 1.98, \( p = 0.18 \)).

The percent of patients with abnormal and normal responses for gait speed were calculated as a function of saccade group (Fig. 3, panel B). In the Covert group, 75% demonstrated normal gait speed (≥1 m/s); whereas, 60% of the Overt group and 62.5% of the Combination group had normal gait speed. No significant difference between the proportion of individuals who had normal preferred gait speed between groups was observed (Fisher’s exact test = 0.88; \( p = 0.89 \)).

The mean 4-item DGI score for the Covert group was 9.0 (2.9), for Overt group was 6.2 (2.9), and for the Combination group was 8.7 (1.5). An ANOVA revealed that there was no significant difference in mean DGI score as a function of saccade group (F(2, 14) = 2.6,
Further, when looking at falls risk based on a cutoff score of \( \leq 9 \) on the DGI (Fig. 4, panel B), there was no significant difference in the proportion of individuals who had scores that were consistent with increased falls risk (Fisher’s exact test = 3.01; \( p = 0.26 \)). In general, the majority of individuals with BVH (75 to 80%) had DGI scores that were consistent with an increased risk of falls.

No significant difference among the groups for self-reported falls was observed (Fisher’s exact test = 2.55, \( p = 0.29 \)) (Fig. 5, panel B); 25% of Covert group reported a fall; whereas, 80% in the Overt group and 57% in the Combination group reported a fall.

**DISCUSSION**

Following the loss of vestibular function, some patients functionally improve and are minimally bothered by their loss of peripheral function while others remain more symptomatic and are unable to return to their typical activities of daily living. We still do not have a deep understanding of the mechanisms for functional improvement. The purpose of the present study was to examine the associations among corrective saccades and measures of handicap, dynamic visual acuity, gait, and falls.

When examining patients with a UVH, we found a significant difference in dynamic visual acuity of individuals with covert only saccades versus those with overt only or a combination of both types of saccades. Similarly, Wettstein (2017) also demonstrated improved dynamic visual acuity with covert saccades. It has been demonstrated that compensatory saccades (i.e., covert saccades; saccades that occur during the head impulse) reduce gaze position error during active and passive head impulses; whereas, corrective saccades (i.e., overt saccades; saccades that occur after the head impulse) do not (Schubert et al. 2010). Thus, compensatory (covert) saccades seem to provide a mechanism to overcome the VOR deficit and improve gaze stability, which may be important to postural stability. Our results also demonstrate differences in gait and fall risk as a function of saccade latency type in the UVH patients. Preferred gait speed was more often normal in those patients with UVH with covert saccades versus those with overt saccades or a combination of both types of saccades. Moreover, patients who demonstrate covert saccades were less likely to be characterized as a falls risk (using a 4-item DGI cutoff of \( \leq 9 \)) compared to those with overt saccades or both. The fact that our findings demonstrate better performance across several domains of physical function measures is important as we consider rehabilitation for these patients. Our work is consistent with prior investigations by Honaker and Shepard (2011) that showed DVA (tested while seated) was a sensitive screening tool to identify individuals with increased fall risk. In our UVH cohort, those with covert saccades demonstrated better DVA and reduced fall risk. Two preliminary studies have demonstrated that vestibular rehabilitation reduced the number and amplitude of overt corrective saccades in UVH patients (Cerchiai et al. 2018; Trinidad-Ruiz et al. 2018). These findings would suggest that future work directed towards targeting exercises that optimizes transition from overt to covert saccades may provide benefit to patients with vestibular hypofunction.
Interestingly, our data failed to demonstrate any statistically significant differences in any of the outcome measures in the BVH group as a function of saccade type. This is surprising as Hermann et al. (2017) reported that covert saccades were positively correlated with dynamic visual acuity. Furthermore, Schubert et al. (2010) demonstrated that patients with BVH tended to use covert (aka, compensatory) saccades more frequently than patients with UVH. When examining our data for BVH patients, there does appear to be a trend towards the group with covert saccades demonstrating better DVA than the overt saccades group; however, the BVH group with both types of saccades had large variability and the differences were not statistically significant. Relative to the other measures of interest (dizziness handicap, gait, fall risk, and history of falls), in general the BVH patients demonstrated moderate or greater perceived handicap, high rates of abnormal gait, and a high rate of falls across all groups. One concern when measuring physical performance in the BVH population is possible floor/ceiling effects. Prior reports of several of the measures show large variability in performance and not necessarily floor and ceiling effects. For example, work by Herdman et al. (2015) shows that 60% of BVH patients have abnormal dynamic visual acuity and gait speed and 77% showed abnormal DGI performance. While there were large numbers of abnormal findings the mean scores would suggest that floor and ceiling effects were not particularly concerning in their population. Similar patterns of findings were reported by Brown et al. (2001) in which DHI (mean = 61, range 22–100) and DGI (mean = 13, range 1–20) scores showed great variability but neither showed clear floor or ceiling effects. It is noted that our study used the four-item DGI rather than the eight-item DGI. It is possible that may have impacted our results; however, results by Marchetti and Whitney (2006) show similar psychometric properties on the four-item measure compared to the eight-item measure. Moreover, it is possible, that we failed to detect a difference due to our small BVH sample size and that our sample included varying degrees of BVH severity. In this study, we utilized our clinical cutoffs for classification of BVH. Not all individuals’ rotary chair results met the Barany Society’s rotary chair criteria (Strupp et al. 2017) for bilateral hypofunction (i.e., our gain cutoff at 0.01 Hz was gain <0.15 whereas the Barany society recommends a cutoff of <0.10). However, all patients met the other components described in the cutoff relative to symptoms (unsteadiness with walking/standing and/ or movement-induced blurred vision/oscillopsia or worsening unsteadiness in darkness and uneven ground and no symptoms while sitting or lying down) and bilaterally absent or reduced VOR function. In that way, it is possible that we have a full spectrum relative to the degree of BVH severity. It is possible that a larger sample size that is powered to detect differences, along with other more sensitive measures of balance and gait may be useful to understand the role saccades may play in the BVH patient population.

There are some limitations of the present study. First, vHIT recordings were not always performed on the same day as the gait and balance measures but were performed within 2 weeks of each other. Our study sample primarily consisted of patients with chronic symptoms with most having an onset greater than a month before evaluation; thus, we do not believe that a delay in assessment would make a significant effect on our findings. Second, although our patients were primarily patients with chronic symptoms, we have not controlled for time since onset of symptoms. Saccade metrics and central compensation mechanisms are influenced by time and should be evaluated in future prospective studies. Third, our study did not account for potential residual function in the other vestibular end-organs (i.e., we did not account for anterior canal, posterior canal, saccule, or utricle function) and focused solely on the groupings based on horizontal semi-circular canal function. It is possible that individuals with residual function in other vestibular end-organs may demonstrate better performance but it is not clear the effect that residual function in other end-organs may play on horizontal canal vHIT saccade latency. Future prospective studies that are capable of controlling for these variables will be necessary. Finally, in the present study, we characterized saccades patterns into three groups based on latency—overt, covert, or combination. Future studies that treat latency as a continuous variable may help to better clarify results of our study and may ultimately be capable of identifying cut-points for degraded function. Present work in this area is underway in our lab.

CONCLUSIONS

Our results show that the presence of predominantly covert saccades is associated with better performance on measures of dynamic visual acuity, gait, and balance in patients with UVH. Patients exhibiting overt saccades or combination of both covert and overt saccades were more often found to have an abnormal gait speed and be characterized as being at risk for falls using the DGI. Our findings suggest that corrective saccade latency is related to measures of physical function. The extent to which saccade latency has the potential to be a useful target for vestibular rehabilitation is still to be determined and may be promising target to improve functional outcomes.

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