Does vestibulo-ocular reflex gain measured by video head impulse test decrease with age?

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INTRODUCTION

The prevalence of dizziness in general practice varies between 1.0 % to 15.5%, of which the most common etiology is vestibular/peripheral (5.4-42.1%) based on a recent systematic review.1 The semicircular canals are the key organs which help to control and maintain balance. The Video Head Impulse Test (vHIT) system is designed to detect semicircular canal dysfunction which can often go undiagnosed during clinical examination of patients with dizziness. The development of objective measurements of the vestibulo-ocular reflex (VOR) in response to natural values of head angular acceleration – the vHIT – has been invaluable in identifying horizontal semicircular canal loss, either unilateral or bilateral.2 Recently, vHIT has been extended to testing vertical canal function, allowing fast, simple and accurate assessment of the functional status of each of the six semicircular canals individually.3,4 vHIT has been validated by direct simultaneous comparison of vHIT with scleral search coils on the same eye of healthy subjects and patients with known vestibular loss, including those after unilateral
vestibular schwannoma operations. The usual measure of performance has been the gain of the VOR, and some values of normal VOR gain, averaged across healthy subjects, have been published. More recently, studies have also determined the normative values for VOR gain in healthy subject in each decade of life. However, these values have limitations: they are based on a relatively small number of subjects and they are not based on an Asian population. The present study aims to overcome some of these limitations.

Several normative studies based on video-analysis of eye responses to head impulses exist. Studies need to account for the well-known factors that influence VOR gain and time constant: target proximity, mental set, active or passive performance, subject age, and velocity of the stimulus. In this study, we would like to address the issue of whether (VOR) gain decreases with age in all 3 semicircular canals.

Our objectives were to determine age-dependent normative values of VOR gain for the vHIT of semicircular canal function in healthy Asian subjects in each decade year of life, and more importantly to examine whether VOR gain measured by vHIT decreases with age.

METHODS

We conducted a prospective cohort study of 60 healthy voluntary community-dwelling subjects, between 21 to 80 years of age. Subjects with prior history of vertigo were excluded. Subjects were recruited through flyers placed on prominent locations in the hospital and were reimbursed $50 each for their participation in the study. All subjects provided written informed consent. The study protocol was approved by the National Health Group Domain Specific Review Board (DSRB). This study was funded by the Alexandra Health Enabling grant (AHEG1625). Subjects were recruited between March 2016 to March 2017. A sample size of 60 was chosen based on previous studies in the literature and also limited by the grant funding.

Video head impulse tests were carried out with the Interacoustics (EyeSeeCam) video goggles. (Figure 1) The subjects were tested in a well-lit room (to ensure small pupil size) with an eye level target of minimum distance of 1m in front of them. The goggles were fitted firmly on the nose bridge and calibrated. The test was performed by one senior audiologist with prior experience with vHIT to ensure consistency in the results. To test the horizontal semicircular canals, the subject was instructed to maintain visual fixation on a target fixed straight ahead with the head pitched downwards approximately 20 degrees. The operator then delivered brief, passive head turns. To test the vertical canals, the head impulses were delivered in the plane of the canal paired under test. The vertical canals are oriented in planes about 45° to the median plane of the head and form two canal pairs – left anterior–right posterior (LARP) and right anterior–left posterior (RALP). To test the LARP canals, the subject was instructed to visually fixate the central fixation point eccentrically. Thus, a diagonal head pitch forward (toward the fixation target) activates the left anterior canal and causes an upward eye movement, and a head pitch back (away from the fixation target) activates the right posterior canal and causes a downward eye movement.

The VOR gain was measured for all six semicircular canals for subjects in decade age bands. Subjects with covert and overt saccades on the vHIT were excluded.

Statistical analysis was performed using Stata (version 13.1, College Station, TX: StataCorp LP), significance tests were 2-sided at the 5% significance level. Data normality was checked using Shapiro-Wilk normality test.

The difference in mean VOR gain, overall and by lateral, anterior and posterior canal between age groups (21-30 versus 31-40 versus 41-50 versus 51-60 versus 61-80 years) was assessed using ANOVA (Analysis of Variance). Further analysis was done to examine p-value for trend using linear regression models to assess if there was a trend in mean VOR gain across the age decades. Paired t-test was used to assess whether right versus left mean VOR gains were different by lateral, anterior and posterior canal. Pearson correlation was used to examine the direction and strength of correlation between age (taken as linear continuous variable) and mean VOR gain. Results are reported as count (n) and percentage for categorical data and mean, standard deviation (SD) for continuous data. Statistics were performed by a statistician.

RESULTS

Sixty subjects were recruited, but only 53 subjects were included in final analysis after excluding 7 subjects.

Table 1: VOR gain by age group.

|                     | Total | 21-30 | 31-40 | 41-50 | 51-60 | 61-80 | P value (ANOVA) |
|---------------------|-------|-------|-------|-------|-------|-------|-----------------|
| Number (%)          | 53    | 13    | 10    | 8     | 10    | 12    |                 |
| Age years, mean (SD)| 45.4  | 26.5  | 34.9  | 44.6  | 55.6  | 66.5  | 0.001           |
|                     | (15.5) | (2.5) | (3.1) | (3.5) | (2.4) | (3.3) |                 |
| Mean VOR gain, mean (SD) | 1.183 | 1.154 | 1.121 | 1.28  | 1.170 | 1.209 | 0.417           |
|                     | (0.190)| (0.202)| (0.207)| (0.164)| (0.224)| (0.144)|                 |

Continued.
Of the 7 subjects that were excluded, 1 withdrew due to the detection of vestibular hypofunction, 2 had overt saccades and 4 had hyper-gain. The mean age of the cohort was 45.4 years. The mean (SD) VOR gain for the cohort was 1.18 (0.19). The mean of the VOR gain for each of the six semicircular canals were analysed to develop a normative guide.

Table 2: Comparison of right versus left VOR gain.

|                      | Mean VOR gain, mean (SD) | P value (paired t-test) |
|----------------------|--------------------------|------------------------|
| Right lateral        | 1.209 (0.323)            | 0.002                  |
| Left lateral         | 1.311 (0.296)            |                        |
| Right anterior       | 1.385 (0.357)            | <0.001                 |
| Left anterior        | 0.990 (0.202)            |                        |
| Right posterior      | 0.879 (0.169)            | <0.001                 |
| Left posterior       | 1.323 (0.352)            |                        |

Table 3: Correlation between age and mean VOR.

|                        | Pearson's correlation coefficient (r) | P-value for correlation |
|------------------------|---------------------------------------|-------------------------|
| Mean VOR gain          | 0.121                                 | 0.389                   |
| Mean VOR gain right lateral | 0.035                              | 0.803                   |
| Mean VOR gain left lateral | 0.066                              | 0.637                   |
| Mean VOR gain right anterior | 0.180                              | 0.196                   |
| Mean VOR gain left anterior | 0.001                              | 0.996                   |
| Mean VOR gain right posterior | 0.029                               | 0.838                   |
| Mean VOR gain left posterior | 0.106                              | 0.447                   |
The mean VOR gain of each decade year was compared to the decade prior. The decades 60-70 years of age and 70-80 years of age were combined for analysis as the latter had only 2 subjects (Table 1). ANOVA showed that the mean VOR gain per decade year did not vary significantly with age. (Figure 2) The ANOVA for the mean VOR gain for the individual canals per decade year also did not vary significantly with age (Figure 3). Interestingly, the paired t-tests in the mean VOR gain showed a significance between the right and left lateral, anterior and posteriorly semicircular canals (Table 2). This is postulated to be due to our audiologist being right handed leading to the difference in values. Pearson's correlation showed that the correlation between age and mean VOR values was negligible and age is unlikely to influence mean VOR gain (Table 3).

With regard to directional differences, our study showed that there was a significant difference for the right VOR gain for all 3 semi-circular canals compared to their matched left semi-circular canals. These findings were similar to McGarvie et al. study in 2015 where this was attributed to only the right eye being measured which was similar to our study. As the head rotates to the right, the right eye has to make a slightly larger rotation within the skull to remain fixated on a target 1 m from the subject, in comparison to the left eye. The effect is reversed for an impulse rotation to the left. This effect has also been confirmed by measuring both eyes with dual search coils, which has shown up to 15% difference in the slope gain between the adducting and abducting eyes at high velocities during head impulses.

Our study aimed to develop normative values for an Asian population by ensuring our subjects had no prior history of vertigo. These subjects were independent, healthy and from the community. Also, we ensured standardization by having the vHIT performed by our one senior audiologist with many years of experience performing the vHIT. We also analysed data in not only the lateral canal but in all 3 semi-circular canals. There were several limitations to our study. Firstly, our numbers were limited mainly by our funding availability. Secondly, it was challenging to recruit subjects who were above 60 with no prior history of vertigo as many of them inevitably would have a previous experience of imbalance or have general medical conditions potentially limiting their involvement.
CONCLUSION

We propose that our normative age-dependent data guide be used to improve the differentiation between normal and abnormal values of VOR gain in an Asian population. This will help guide us for determining patients with vestibular hypofunction, especially those with bilateral vestibular hypofunction. Our study shows that VOR gain, as measured directly by the eye movement response to head rotation, seems largely unaffected by aging. Therefore allowing the normative values to be extended throughout the age groups.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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