INTRODUCTION
The vestibulo-ocular reflex (VOR) assists in steadying images on fovea when there is any movement of the head. The head and eye moving at the same time is considered ideal VOR gain. In such a situation, it will produce eye rotations at a speed similar to the head rotation but in an opposite direction. It will not be connected to the temporary rotation axis of the head [1]. A number of factors are thought to impact VOR considerably; among these are vision, cervical proprioceptors, cerebellum, and cortical input by central pre-programming system [2-11]. Past experiments have also suggested that the vestibular system is able to identify and differentiate between active and passive head movements, even at the vestibular nuclei level [12].

The vestibulo-ocular reflex is measured by the video head impulse test (vHIT). The vHIT consists of specific software and lightweight goggles that have an eye position camera and a gyroscope. The camera follows the path taken by the pupils of the eye, and the gyroscope tracks the head movements and computes VOR gain [13]. The vHIT evaluates the gain and saccades of the eye. The camera that was used in this work was a monocular high-speed camera with the speed of 150-250 Hz for eye video recordings and an angular velocity sensor to measure the pace of head movements in all three dimensions.

OBJECTIVE:
The objective of this study was to establish which factor leads to a higher vestibulo-ocular reflex (VOR) gain: the timing of the movement or the direction of the movement. For this purpose, healthy volunteers were examined under three conditions: (1) when they were informed about the timing of the head movement; (2) when they were informed about the direction of the head movement; and (3) when they knew both the timing and the direction of the head movement.

MATERIALS and METHODS:
This study included data from 19 participants between the ages of 20 and 23 years with no neurological or vestibular ailments. The gains of the video head impulse test (vHIT) were measured under four different conditions and the final control tests. Five subgroups were defined, and the differences in the subgroups were assessed with using several statistical procedures.

RESULTS:
We found that there were significant differences between all subgroups gains on the right and left head rotations. Nevertheless, non-significant differences were found by performing independent samples t-tests and Mann-Whitney U tests between left and right head rotations for the pairwise comparisons of subgroups. Also, analysis of variance (ANOVA) results indicated that vHIT gains for the right and left, respectively. Thus, knowing the timing or direction or both does not affect vHIT gains.

CONCLUSION:
The results of these experiments revealed that there is no association whatsoever between VOR gain and awareness of the timing or direction of the movement or both.

KEYWORDS:
Vestibulo-ocular reflex, video head impulse test, VOR gain, eye velocity
The vestibulo-ocular reflex gain can be put in equation form as the following:

\[ \text{VOR gain} = \frac{\text{Eye movement velocity}}{\text{Head movement velocity}}. \]

The VOR is, thus, the ratio of slow phase eye velocity to head velocity. There is no uniformity on how much VOR gains should be since there is very little experimental data to fix its normative values. It is generally expected to be 1, but in reality, participants in studies on this subject have VOR gains ranging between 0.8 and 0.9. However, a few studies have set the VOR gain range to be above 1.

If VOR is due to afferent causes, the resultant active and passive high frequency rotations may be different (active rotations refer to those that are self-generated and passive rotations refer to those that are created manually). Past investigations have suggested that VOR gains seem to be higher in predictable conditions that result in active head rotations. Studies have shown, surprisingly, that in cases of passive head and body rotation, the resultant gain was higher than 1, more than in active head rotation. Conjectures have been made regarding this occurrence, but it is still not certain why this happens in passive whole body rotation. Even if bilateral acoustic neuromas were removed, a gain of 0.4 is observed. This has led researchers to believe that other mechanisms such as central pre-programming and neck afferents lead to a higher VOR in such patients.

This study was conducted to establish which factor leads to higher VOR gain: the timing of the movement or the direction of the movement.

**MATERIALS and METHODS**

**Participants**

The 19 participants chosen for this study were healthy subjects with no neurological or vestibular ailments. They were between 20 and 23 years old (with a mean age of 21.84 years). There were 6 male participants and 13 female participants. The study was approved by the ethics committee of our institution. All procedures were explained to the participants before testing, and informed consent was obtained from all participants.

**Protocol**

To determine the premise, the ICS Impulse version 3.0 vHIT test system by GN Otometrics of Denmark was employed. The subjects were tested with lateral vHIT under five conditions that are listed below:

1. Under normal vHIT testing, the subjects were unaware of the timing or the direction of the head movement (subgroup 1).
2. The subjects were not told about the timing but informed about the direction of the head movement (subgroup 2).
3. The participants were informed about the timing by telling the participants before the movement of the head by saying “now.” However, the participants were clueless about the direction the head was rotated to (subgroup 3).
4. The subjects conducted the tests themselves and thus were aware of both the timing and the direction of the head movement (subgroup 4).
5. The subjects were control tested under lateral vHIT without knowing the direction or timing of the head movement (subgroup 5).

**Statistical Analysis**

After the experiments were completed, the gains of vHIT were used to calculate descriptive statistics of the test results (mean±standard deviation). Then statistical analysis was performed by separating the data into five subgroups as mentioned in protocol.

Once the descriptive statistics were completed, other sophisticated statistical methods were employed to assess the differences, if any, among or within the groups. Some of the procedures used included the Mann-Whitney U test, one-way analysis of variance (ANOVA) test, independent samples t-test, and Kruskal-Wallis H test.

Past studies have utilized the independent samples t-test or Mann-Whitney U test for comparing two separate groups based on their means. What mainly differentiates these two tests is hypothetical data normality. The parametric independent samples t-test is employed if the data distribution is normal. If the data distribution is not normal, then the Mann-Whitney U test is used. This test is the nonparametric alternative test for the independent samples t-test. Depending on the requirement, the independent samples t-test or Mann-Whitney U test were used. Within each subgroup, these tests helped establish the statistical differences between both the directions. Each subgroup was tested for two hypotheses: null (H0) and alternative (H1). While the null hypothesis states that the mean values of two subgroups are similar, the alternative states that the mean values are not the same.

If there were more than two independent groups being studied, then the ANOVA and Kruskal-Wallis H tests were employed for comparison. ANOVA is the parametric test used and Kruskal-Wallis H its nonparametric alternative that does not require the normal distribution assumption that ANOVA requires. As in the tests for finding differences between two subgroups, two hypotheses (H0; H1; at least one subgroup is different in terms of its mean) were tested.

Statistical procedures were used only after the Kolmogorov-Smirnov or Shapiro-Wilk normality tests were conducted. Based on the ensuing results, a decision was made about whether parametric or nonparametric procedures would be more suitable to reach a conclusion. Statistical Package for Social Sciences software (IBM Corp.; Armonk, NY, USA) was used in order to perform the statistical analyses.

**RESULTS**

Differences in the subgroups were evident from the readings obtained. Detailed descriptive statistics of raw data are shown by Table 1. As seen in Table 1, in subgroup 1, the normal vHIT gain was 0.943±0.068 on the right and 0.901±0.078 on the left. Results of subgroup 2 showed direction vHIT gains of 0.948±0.079 and 0.875±0.072 for the right and left directions, respectively. Subgroup 3 showed gains of time vHIT of 0.931±0.082 and 0.872±0.080 in the right and left directions, respectively, and includes both minimum and maximum gain values of all subgroups. Readings from subgroup 4 showed the mean and standard deviations for gain in self vHIT as 0.951±0.066 and 0.876±0.035 for the


differences between subgroups; HA: at least one subgroup is different from all participants.

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- Readings from subgroup 4 showed the mean and standard deviations for gain in self vHIT as 0.951±0.066 and 0.876±0.035 for the
Table 1. Descriptive statistics of raw data

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Min. / Max.</th>
<th>Range</th>
<th>Skewness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right direction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subgroup 1</td>
<td>0.943</td>
<td>0.068</td>
<td>0.76/1.04</td>
<td>0.28</td>
<td>-1.294</td>
</tr>
<tr>
<td>Subgroup 2</td>
<td>0.948</td>
<td>0.079</td>
<td>1.12/0.79</td>
<td>0.33</td>
<td>0.234</td>
</tr>
<tr>
<td>Subgroup 3</td>
<td>0.930</td>
<td>0.082</td>
<td>1.04/0.80</td>
<td>0.34</td>
<td>1.032</td>
</tr>
<tr>
<td>Subgroup 4</td>
<td>0.951</td>
<td>0.066</td>
<td>1.06/0.79</td>
<td>0.27</td>
<td>-0.595</td>
</tr>
<tr>
<td>Subgroup 5 (control)</td>
<td>0.956</td>
<td>0.077</td>
<td>1.13/0.79</td>
<td>0.34</td>
<td>0.496</td>
</tr>
<tr>
<td>Left direction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subgroup 1</td>
<td>0.901</td>
<td>0.078</td>
<td>1.08/0.79</td>
<td>0.29</td>
<td>0.905</td>
</tr>
<tr>
<td>Subgroup 2</td>
<td>0.875</td>
<td>0.072</td>
<td>1.04/0.75</td>
<td>0.29</td>
<td>0.219</td>
</tr>
<tr>
<td>Subgroup 3</td>
<td>0.872</td>
<td>0.080</td>
<td>1.06/0.73</td>
<td>0.33</td>
<td>0.451</td>
</tr>
<tr>
<td>Subgroup 4</td>
<td>0.876</td>
<td>0.035</td>
<td>0.93/0.78</td>
<td>0.15</td>
<td>-0.871</td>
</tr>
<tr>
<td>Subgroup 5 (control)</td>
<td>0.901</td>
<td>0.066</td>
<td>1.09/0.75</td>
<td>0.34</td>
<td>0.698</td>
</tr>
</tbody>
</table>

Min: minimum; max: maximum

Table 2. Results for right and left directions for all subgroups

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Test value</th>
<th>p</th>
<th>Statement of null hypothesis</th>
<th>Decision (differences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup 1 Mann-Whitney U</td>
<td>104.500</td>
<td>0.026</td>
<td>Rejected</td>
<td>Significant</td>
</tr>
<tr>
<td>Subgroup 2 t-test</td>
<td>2.929</td>
<td>0.006</td>
<td>Rejected</td>
<td>Significant</td>
</tr>
<tr>
<td>Subgroup 3 t-test</td>
<td>2.218</td>
<td>0.033</td>
<td>Rejected</td>
<td>Significant</td>
</tr>
<tr>
<td>Subgroup 4 Mann-Whitney U</td>
<td>56.000</td>
<td>0.000</td>
<td>Rejected</td>
<td>Significant</td>
</tr>
<tr>
<td>Subgroup 5 Mann-Whitney U</td>
<td>83.000</td>
<td>0.004</td>
<td>Rejected</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Table 3. Results for pairwise comparisons of subgroups

<table>
<thead>
<tr>
<th>Subgroups (vs.)</th>
<th>Procedure</th>
<th>Test value</th>
<th>p</th>
<th>Statement of null hypothesis</th>
<th>Decision (differences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right direction</td>
<td>1 vs. 2 Mann-Whitney U</td>
<td>175.000</td>
<td>0.872</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>1 vs. 3 Mann-Whitney U</td>
<td>131.000</td>
<td>0.147</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>1 vs. 4 Mann-Whitney U</td>
<td>170.500</td>
<td>0.770</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>1 vs. 5 Mann-Whitney U</td>
<td>122.900</td>
<td>0.969</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td>Left direction</td>
<td>1 vs. 2 t-test</td>
<td>1.028</td>
<td>0.311</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>1 vs. 3 t-test</td>
<td>1.126</td>
<td>0.268</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>1 vs. 4 Mann-Whitney U</td>
<td>156.500</td>
<td>0.481</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>1 vs. 5 t-test</td>
<td>-0.044</td>
<td>0.965</td>
<td>Not rejected</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

Table 4. Results for all subgroups

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Procedure</th>
<th>Test value</th>
<th>p</th>
<th>Statement of null hypothesis</th>
<th>Decision (differences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right direction</td>
<td>Between all subgroups</td>
<td>Kruskal-Wallis H</td>
<td>2.579</td>
<td>0.631</td>
<td>Not rejected</td>
</tr>
<tr>
<td>Left Direction</td>
<td>Between all subgroups</td>
<td>ANOVA</td>
<td>0.742</td>
<td>0.566</td>
<td>Not rejected</td>
</tr>
</tbody>
</table>

Yilmaz et al. Time and Direction Information
experimental studies by Sprenger et al. \(^2\) yielded different results. Not only do they demonstrate that light plays an important role in VOR gain in healthy individuals, but they also show that, compared with unpredictable ones, there is higher VOR gain in predictable tests.

This is so because, according to the researchers, other factors help increase VOR gain during active head movements. These factors include predictable pre-programmed responses that are fundamentally connected with active head impulses in individuals and the predicted neck proprioceptive afferents that may be terminated during active head movements.

Interesting outcomes have resulted from studies conducted by Black et al.\(^1\) on six subjects with total unilateral vestibular deafferentation that occurred years after vestibular schwannoma (acoustic neuroma) surgery. The researchers studied VOR gain in these subjects with both active and passive head impulses. Their results showed that VOR gain was considerably abnormally low with both conditions. With active head impulses, it was seen to be almost twice than that of passive head impulses. The researchers suggest that this could be because the subjects may have been able to predict their gaze error, following which they may have made compensatory express saccades in time with their head rotations.

Migliaccio and Schubert \(^3\) suggest that with as little as 15 minutes of tutoring, unilateral incremental VOR adaptation can be stimulated in normal subjects. Their experiments showed that during active head impulses, VOR gain in the adapting direction was increased by -22% and by -11% during passive ones. This proves that it is not only due to training that changes occur in the predictive eye movement mechanisms that receive efferent copy signals of internal motor commands; it is also due to the variable VOR pathways.

These findings raise two more questions. First, is pre-programming found only in patients with vestibular ailments? Second, is pre-programming a fact and does it even exist? These questions can possibly be answered by further research in the subject.

The vestibulo-ocular reflex testing is done by employing the vHIT. Although not much research has been done in setting normative values, VOR gain in healthy normal individuals is considered to be approximately 1 \(^4\). However, a few studies accept the value of normal VOR to be higher than 1. Studies show that VOR does not only stem from semicircular canals but also can arise from varied afferent inputs; the gains from predictable and unpredictable head movements, though, contributions may be different.

In this study we found that there is a significant difference between gains on the right and left direction head movements. This could be due to the fact that the right brain dominancy or any other unknown factors exists. Also, one other bias for the tests were informing the participants for the time domain. This was done by informing the participant by saying "now," which meant that it was time for the tester to begin the head movement. However, in this case, we could not take in to account the timing between saying "now" and the beginning of the movement. This might affect central pre-programming.

As is evident from the results of the various tests done, awareness of the participant with regard to the direction, timing, or both does not lead to any substantial VOR gain changes, thus leading to the conclusion that central pre-programming does not lead to significant improvements in VOR gains. However, this can also be dependent on the normal vestibular system responses of the participants.

**Ethics Committee Approval**: Ethics committee approval was received for this study from the ethics committee of Istanbul Medipol University on 03.22.2017 with decision no:108 and number 10840098-604.01.01-E.8318.

**Informed Consent**: Written informed consent was obtained from patients who participated in this study.

**Conflict of Interest**: No conflict of interest was declared by the authors.

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**REFERENCES**

1. Fetter M. Vestibulo-ocular reflex. Germany: Karger; 2007. [CrossRef]
4. de Jong PTVM, de Jong JMBV, Cohen B, Jongkees LB. Ataxia and nystagmus induced by injection of local anesthetics in the neck. Ann Neurol 1977; 1: 240. [CrossRef]
11. Markham CH. Descending control of the vestibular nuclei: physiology. Prog Brain Res 1972; 37: 111-7. [CrossRef]
Curthoys IS. The video head impulse test (vHIT) of semicircular canal function- age-dependent normative values of VOR gain in healthy subjects. Frontiers in Neurology 2015; 154: 1-11. [CrossRef]


17. Della Santina CC, Cremer PD, Carey JP, Minor LB. Comparison of head thrust test with head autorotation test reveals that the vestibulo-ocular reflex is enhanced during voluntary head movements. Arch Otolaryngol Head Neck Surg 2002; 128: 1044-54. [CrossRef]


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