



Original Article

# Normal Gain of VOR with Refixation Saccades in Patients with Unilateral Vestibulopathy

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**OBJECTIVE:** To characterize the response in the video head-impulse test for the assessment of the vestibulo-ocular reflex (VOR) in patients because of vertigo and dizziness.

**MATERIALS and METHODS:** After rightward and leftward head impulses, the following results evaluated were: gain of the reflex and appearance of refixation saccades. A particular type of response (normal gain VOR and refixation saccades) was evaluated in a group of patients.

**RESULTS:** In patients with a unilateral abnormality consisting of normal gain and refixation saccades, there was a close concordance with the diseased side and the side to which head impulses elicited the abnormal result.

**CONCLUSION:** In the assessment of patients with dizziness, finding a normal gain VOR with refixation saccades indicates the existence of a peripheral vestibulopathy and localizes to the side of the lesion.

**KEYWORDS:** Vertigo, dizziness, inner ear, vestibular tests

## INTRODUCTION

The clinical and instrumental examination of the vestibulo-ocular reflex (VOR) is a key issue for the differential diagnosis of patients with dizziness<sup>[1]</sup>. A sudden head thrust of high velocity (>150°/s) and acceleration (1–16 Hz) on the yaw axis stimulates the horizontal semicircular canal receptor of the side to which the impulse is directed. This generates a reflexive eye response that in a normal subject occurs with a latency of 5–7 ms and drives the eye in the opposite direction to that of the head at a similar velocity so as to keep the vision on target. Observing the eye position at the end of the head impulse is the basis of the bedside or clinical head-impulse test (cHIT) that allows for the localization of a vestibular deficiency<sup>[2]</sup> and diagnosis in patients with acute and chronic dizziness.

Patients with a peripheral vestibular deficiency show reduced eye velocity in response to head movements and consequently, a retinal slip during head motion, which is one of the more effective error signals that drive adaptation on VOR<sup>[3]</sup>. This can be accomplished using corrective and compensatory saccades to augment the reduced slow-phase component of VOR<sup>[4,5]</sup>. These saccades occur early, while the head is still in movement, or late, once the head impulse has stopped; in both cases, a certain degree of expertise is needed to correctly evaluate them<sup>[6]</sup>. Alternatively, in a more precise method, by analyzing the velocity profile of the head and eye throughout the head impulse and after it finishes, it is possible to measure the gain of the reflex and register these eventual eye movements, which are also called refixation saccades (RS).

In a clinical setting, new video-based equipment has recently been introduced, which enables registration of the eye in response to sudden head impulses<sup>[7-9]</sup>. This is called the video head-impulse test (vHIT). In a group of normal subjects and patients with vestibular neuritis, it mimicked the performance of the scleral search coil (SSC) in a magnetic field installation<sup>[10]</sup>. This system seems to work not only for the initial evaluation of the vast majority of dizzy patients<sup>[11]</sup> but also for follow-up<sup>[12]</sup>.

The purpose of this work was to evaluate the findings in vHIT in patients with dizziness of peripheral etiology. In particular, we were interested in defining whether the occurrence of RS alone has a localizing value.

This study was presented at the 64<sup>th</sup> Meeting of the Spanish Ear Nose Throat Society (SEORL), 25-28 October 2013, Madrid, Spain.

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**MATERIALS and METHODS**

**Patients**

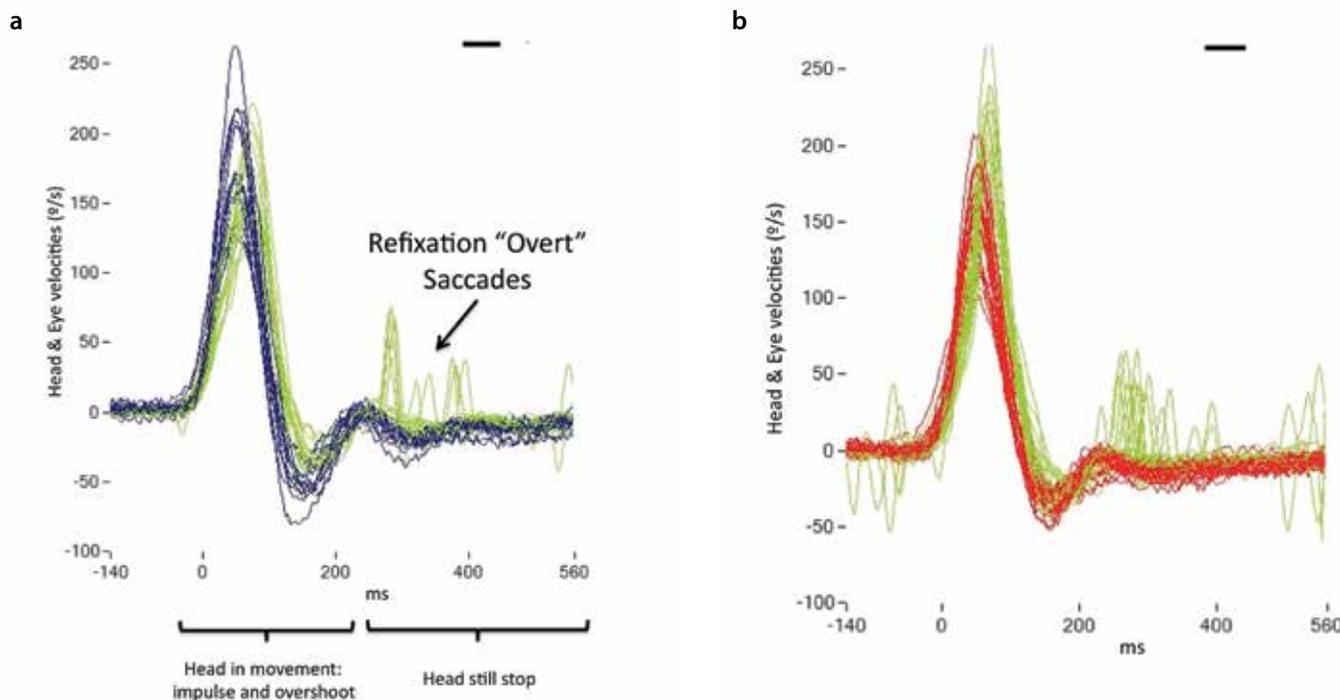
Over a one-year period, 623 patients were included. After an initial basic otoneurological examination, other hearing and vestibular tests and radiographic evaluations were performed to obtain a definite diagnosis. All patients signed informed consent to allow us to use their data in this prospective research.

As the purpose of the study is to assess both VOR gain and RS in patients with unilateral vestibulopathy, some exclusion criteria were developed: 1) central vestibulopathy, 2) a test incompletely performed (fewer than 8 impulses in the rightward or leftward head direction) or with a high variability between each response to the impulse (standard deviation of the collected VOR gains in each patient of >0.2 after leftward and rightward head impulses), 3) gain of VOR below 0.8 for leftward or rightward head impulses, and 4) RS after rightward and leftward head impulses. From the initial database, we constructed a final database including only patients in which normal gain (gain of VOR>0.8) and RS with latency below 170 ms after head velocity reached zero [4] after impulses to only one side. The ethics committee of the hospital approved and supervised the study.

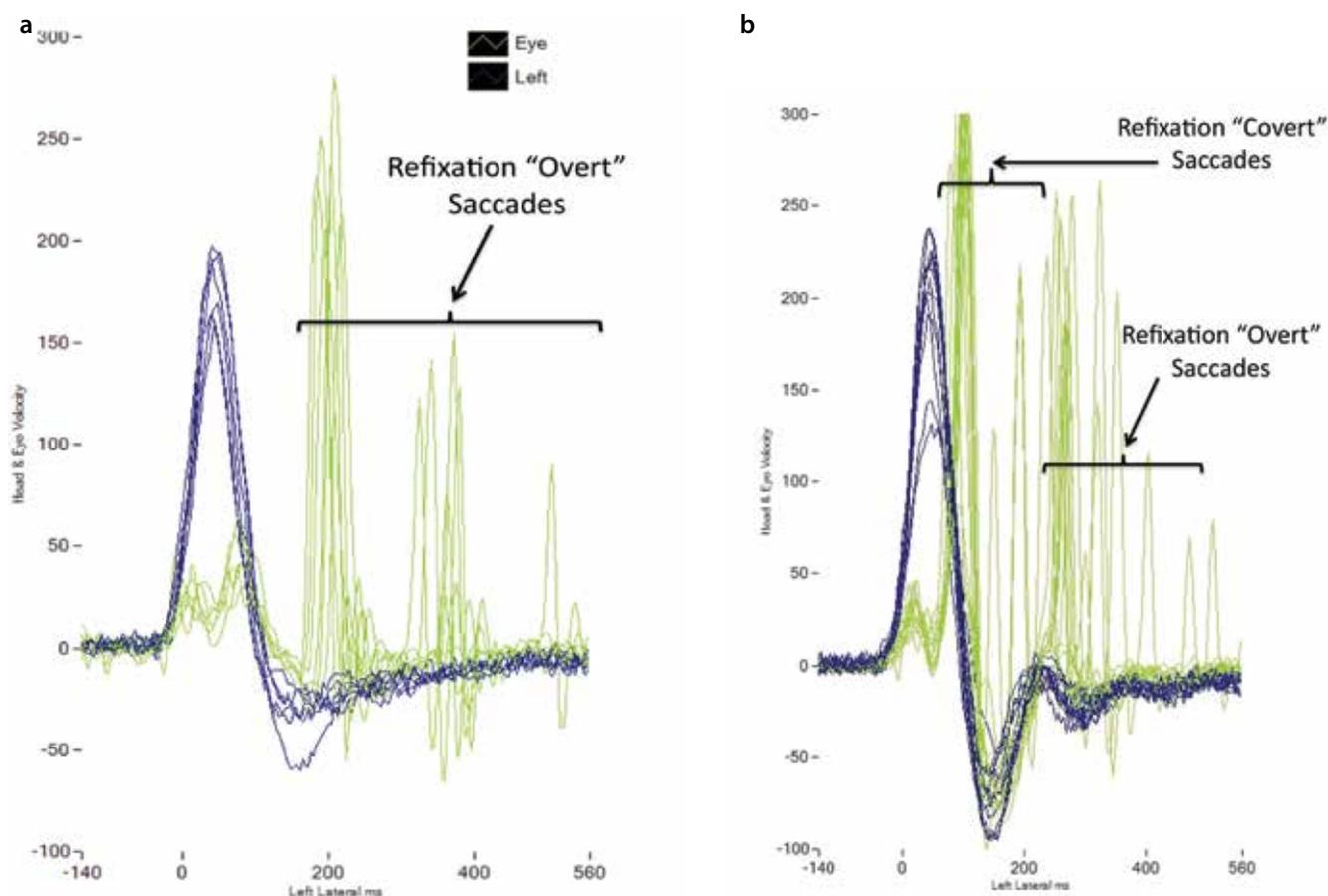
**VOR evaluation**

It was performed with a video system (vHIT GN Otometrics, Denmark). For this test, the patient wore a pair of lightweight, tightly-fitting goggles on which a small video camera and a half-silvered mirror, which reflects the image of the patient's right eye into the camera, were mounted. The eye was illuminated by a low-level infrared light-emitting diode. A small sensor on the goggles measured

the head movement. The whole goggle system weighed approximately 60 g and was tightly secured to the head to minimize goggle slippage. Calibration was performed, and the procedure of vestibulo-ocular testing was initiated. The clinician asked the patient to keep staring at an earth-fixed target 1 m in front, and gave the patient brief, abrupt, and horizontal head rotations through a small angle (approximately 10–20°), unpredictably turning to the left or right in each trial. At the end of each head turn, the head-velocity stimulus and eye-velocity response were simultaneously displayed on the screen. In a full test, 20 impulses were randomly delivered in each direction. At the end of the full test, all head velocity stimuli and eye velocity responses were displayed on a computer screen, together with a graph of the calculated VOR gain (ratio of eye velocity to head velocity) for every head rotation. The parameters evaluated were the VOR mean gain and the appearance of RS after head impulses to the right and left. The mean gain was obtained from the gain value after each of the impulses performed and was automatically provided for rightward and leftward head impulses. Saccades were considered only if systematically found in all impulses in one direction or at least in 80% of the head impulses performed. Physiological saccades were randomly registered throughout the procedure, before or after the head impulse, with a peak velocity of <50°/s, and in a given patient in the evaluation of rightward and leftward impulses (Figure 1); in this case, the gain for leftward head impulses was higher than expected and it could be due to a manifestation of an active ear disease (Meniere's disease) or moderate slippage of the goggle. Pathological or RS was classified as "covert" if they were found while the head was still moving in the impulse, "overt" if they were immediately found after the head stops, and "covert & overt" if both, covert and overt, were found (Figure 2). All patients signed the informed consent form for the test.



**Figure 1. a, b.** Results in vHIT after impulses to the right (a) and left (b) in a patient with probable Meniere's disease in his left ear. In red and blue, rightward and leftward head velocity respectively for different impulses and in green the eye velocity profile. Low velocity saccades are seen before and after head impulse to both sides despite a perfectly matched eye response: mean gain for rightward head impulses was 0.98±0.05 and for leftward head impulses was 1.03±0.06



**Figure 2. a, b.** Results in the leftward vHIT in two patients; in blue leftward head velocity and in green the eye velocity profile for different impulses. (a): patient 2 was diagnosed and surgically treated (translabrynthine removal) for a left vestibular schwannoma 4 years before the test; the mean gain of leftward head impulses was  $0.18 \pm 0.1$ , and refixation saccades are seen once the head movement finished (overt saccades). (b): patient 3 suffered a left temporal bone fracture; the mean gain of leftward head impulses was  $0.21 \pm 0.08$ , and refixation saccades are seen while the head is moving (covert saccades) and once the head movement finished (overt saccades)

### Statistical Analysis

All data were stored and analyzed in an SPSS file, version 19.0 (SPSS Inc.; Chicago, IL, USA). The distribution of continuous variables was evaluated using Shapiro–Wilk test. Data were expressed as mean  $\pm$  standard deviation (SD). The means of the gain of VOR were compared with Wilcoxon test.

### RESULTS

The final population included 36 patients. The diagnoses were as follows: Meniere’s disease in 29 patients, previous vestibular neuritis in 4, post-concussion in 1, vestibular associated otosclerosis in 1, and vestibular schwannoma in 1. The right side was affected in 17 patients and the left side in 19. The mean canal paresis (performed in all patients) was 37% (min: 4%, max: 100%), and the caloric test was considered to be normal (canal paresis <20% and directional preponderance <28%) in 40% of the patients.

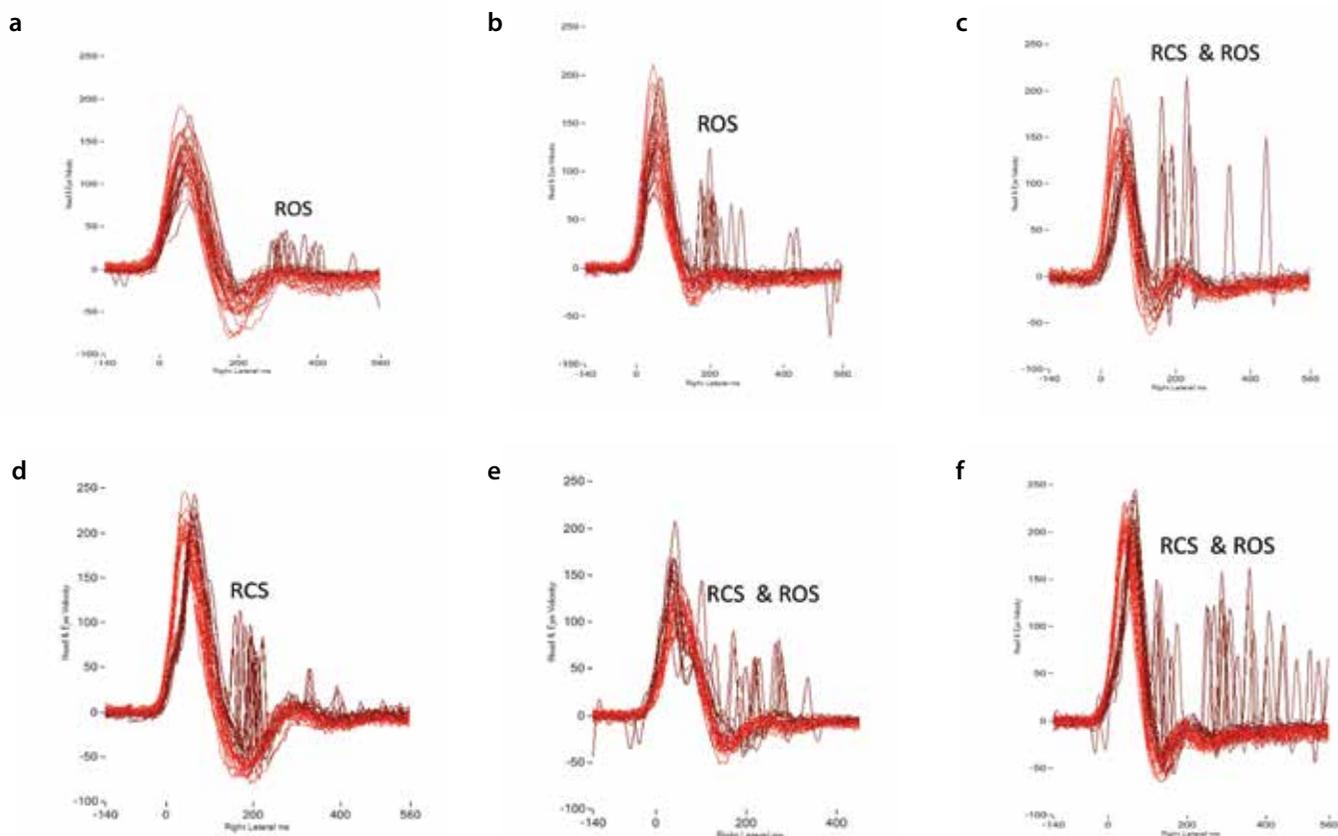
The types of findings are summarized in Figure 3. Different types of findings are shown: only overt saccades were found in 24 (67%) patients, and covert and overt saccades were found in 12 (33%).

In Figure 4, we present the existence of coincidences between side identification by the clinical data and vHIT. In 3 patients, there was no

coincidence between the side as clinically defined and that obtained in vHIT: they were all diagnosed with Meniere’s disease and shared the following characteristics: early onset (disease duration less than 2 years), mild hearing loss in the side of the disease (the mean pure tone average was <30dB), no Tumarkin spells, and the functional level score was less or equal to 2 in all. In one patient, hearing loss was higher in the clinically normal ear, and VEMPs were also abnormally low in that ear. After excluding these 3 patients, gain of VOR was  $0.92 \pm 0.02$  for ipsilesional impulses and  $1.04 \pm 0.02$  for contralateral impulses; differences were significant (Wilcoxon signed-rank test,  $z = -3.7$ ,  $p = 0.001$ ).

### DISCUSSION

The registration and measurement of the eye response to rapid head thrusts with vHIT is an innovation in the evaluation of dizzy patients that can be routinely used in clinical settings<sup>[13]</sup>. It derives from the less clinically available VOR assessment with SSC. It provides information of angular VOR function for high frequency and velocity stimulations that are otherwise physiological; because of this the information gathered during vHIT differs from that obtained in the caloric and rotatory chair testing of the horizontal angular VOR. This was the plane of VOR assessment on which we have concentrated our work, although it is possible to extend this evaluation to other planes.



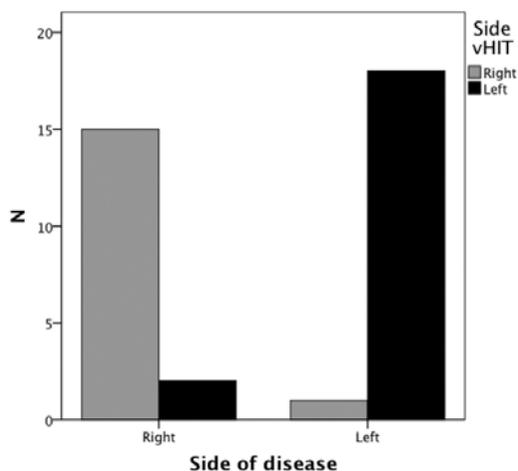
**Figure 3.** a-f. Examples of findings in vHIT (only right-sided results are shown). Several impulses were collected: in red rightward head impulse velocity, and in maroon the eye velocity profile after each head impulse. Overt saccades (ROS) found respectively in 13 patients (a), in 7 (b) and in 5 (c). Covert saccades with (RCS&ROS) or without (RCS) overt in 11 patients (d-f)

In our study we have set a normal gain result above 0.8 in accordance with some previous data<sup>[10]</sup> and our results in a population (N=35) of normal subjects. The second variable under evaluation is rapid eye movements that occur during the test. Some of them can be physiological as seen when trying to fixate on an object of interest. In that situation, even if the head of the subject is well stabilized, it is possible to observe in the eye a high-frequency and low amplitude tremor, slow drift and small saccades which disrupt gaze<sup>[14]</sup>. These microsaccades, also called fixational saccades, are rapid, jerky eye movements smaller than 15 minutes of arc, that follow the main sequence and, with a velocity <50°/s<sup>[15]</sup>. In the unrestrained head condition, as in our study, they are irrelevant but still occur<sup>[16]</sup>. Because of this, we decided to include some criteria to rule them out. Apart from velocity, we were interested in constancy, which means that they were found throughout the testing, as when performing impulses to one or the other side, and in at least 80% of the impulses registered. It must be stressed that overt saccades are frequently seen in normal subjects in particular if they are >71 years old and are dependent of the head impulse velocity<sup>[17]</sup>. For this reason it is desirable to perform a detailed assessment of ocular motility before the vHIT in order to analyze physiological saccades, saccadic intrusions and of spontaneous nystagmus.

Saccades that occur in patients with a normal gain have been shown by previous authors using the vHIT, and in dual studies also with SSC<sup>[7]</sup>. In particular, the work from studies with SSC provides some information on this topic. After an acute vestibulopathy, throughout the

follow-up, the recovery of the ipsilesional gain of VOR has been observed, contrary to what occurs after vestibular neurectomy<sup>[18, 19]</sup>. RS also change during this period, but the type of modification depends on how the evaluation is performed or whether it is in active (the patient performs the head impulse) or passive (the tester performs the impulse). In the former situation (as was the case in our study), only the velocity and latency are reduced from a mean value of 133°/s to 90°/s and 95ms to 75ms, respectively<sup>[20]</sup>. Thus, it is expected that at some time of the recovery period, it would be possible to obtain a normal gain VOR with RS in the head impulse test<sup>[21]</sup>.

We do not consider that this finding is an artifact while testing or an error of analysis for the following reasons. First, because of the selection of the findings that were abnormal results for impulses to just one side, the result after impulses on the contrary being totally normal (normal gain and without RS): this rules out the possibility of an artifact due to the slippage of the goggles. This is reinforced by the methodology of testing as we perform it by attempting to make the impulses unpredictable in time, velocity, and side in such a way that the patient cannot predict the type of impulse he/she will receive. Another source of error, as are blinks, were excluded as they appear in the registry: while testing, the examiner is looking at the response not only as the velocity curve but also at the real eye image allowing to identify and exclude from the analysis blinks that distort VOR if the algorithm included in the system has not already done so. Second, the different types of saccades registered according to their latency and velocity rule out an error of computing the eye velocity. We have



**Figure 4.** Correlation of clinical pathological and abnormal sides according to vHIT

shown that the response is quite heterogeneous but in each patient is consistent for most of the impulses. To characterize and quantify the finding, we chose a classification that can be considered rather artificial and that is based on the findings at the first 200 ms after the initiation of the head impulse and extends the period of assessment up to 200 ms after the termination of head movement. Third, the correlation between the side clinically suspected and where the response was abnormal appeared in all patients but three. They were all diagnosed with Meniere's disease, raising the problem of the existence of a bilateral disease or an unexpected abnormality in the supposedly normal ear. Finally, the differences obtained in gain for impulses with and without RS in the same patient are statistically significant, which means that some degree of damage must have been inflicted or is ongoing in the side in which the impulse generates a normal value gain with RS.

A word of caution must be given as the number of patients with Meniere's disease is very high in the third study, and it deals with the dynamics of gain modification according to the stage of the disease and the amount of time since the last vertigo spell. Using head impulses for the assessment of VOR with a similar methodology as ours in patients in an early stage of the disease, it has been published that while in the quiescent period of the disease, gain is enhanced, in the attack and close to it is reduced<sup>[12]</sup>. These findings do not agree with those obtained in caloric and rotatory chair tests<sup>[22]</sup> due to the different nature of the stimulus and response under analysis in each methodology of horizontal angular VOR assessment.

In conclusion, normal gain with RS is not an artifact but a well-characterized finding in clinical settings.

**Ethics Committee Approval:** Ethics committee approval was received for this study (CUN-15-2012).

**Informed Consent:** Written informed consent has been obtained from all participants.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - N.P.F.; Design - N.P.F., P.E.N.; Supervision - N.P.F.; Materials - N.P.F.; Data Collection and/or Processing - P.E.N.; Analysis and/or Interpretation - N.P.F., P.E.N.; Literature Review - N.P.F., P.E.N.; Writing - N.P.F., P.E.N.

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

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