Perception of Verticality in Patients with Primary Headache Disorders

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OBJECTIVE: Migraine is associated with several vestibular syndromes, and vestibular syndromes can cause tilt of the subjective visual vertical (SVV).

MATERIALS and METHODS: Caloric tests, cervical vestibular evoked myogenic potentials (cVEMPs), and SVV deviations were studied in a group, including 20 patients with migraine without aura (MoA), 24 patients with vestibular migraine (VM), 20 patients with tension-type headache (TTH), and 30 healthy controls. SVV deviations were measured using a translucent bucket. The procedure was repeated 10 times, and the mean SVV deviation was calculated for each subject.

RESULTS: Apart from 5 patients with VM, the caloric test results were normal. cVEMP latencies, amplitudes, and SVV deviation values measured from the patient groups were not statistically different from the healthy controls. Despite not having differences in the average SVV deviation compared to controls, patients with migraine, either associated with vertigo or not, had significantly larger variability in their SVV measurements when all 10 test trials were taken into consideration.

CONCLUSION: The larger variability of SVV measurements in our patients with migraine has also been reported in a previous study. It is difficult to interpret this finding as evidence of vestibular dysfunction involving the otolithic pathways. Cognitive processes affecting the awareness of body orientation seem to be a more reasonable explanation. On the other hand, the bucket method is an easily performed, reliable bedside test to study SVV.

KEY WORDS: Subjective visual vertical, migraine without aura, vestibular migraine, tension type headache

INTRODUCTION
Pathological tilt of the subjective visual vertical (SVV) is accepted as a sensitive sign of vestibular tone imbalance in the roll plane and occurs with peripheral and central vestibular lesions from the labyrinth to the vestibular cortex [1]. It has been shown that healthy participants make errors well within 2 degrees to either side [2]. The static SVV is considered to be a functional measure of otolith-mediated verticality perception, although vertical semicircular canals, in particular, the posterior canal, may also contribute [3]. Standard methods that are used to test for SVV, such as the hemispheric dome method and the light bar in the dark method, require expensive and stationary equipment, as well as experienced operators. A practical and reliable bedside method that can be used to determine the SVV has been introduced and validated by Zwergal et al. [4] that uses a translucent bucket.

Migraine has long been recognized to be associated with several vestibular syndromes, including vertigo, motion sickness, and balance disorders [5-10]. There are several reports about the association of migraine with vertigo; in fact, recent epidemiological data indicate that migraineur vertigo is the second most frequent cause of recurrent vertigo [11]. The pathogenesis is uncertain, but migraine mechanisms may interfere with the vestibular system at the labyrinth, brainstem, and cerebral cortex [7, 8]. Inevitably, several studies have been performed to assess vestibulo-ocular, vestibulo-collic, and vestibulospinal functions in patients with migraine by using caloric tests, cervical vestibular evoked myogenic potentials (cVEMPs), and posturography, with results indicating peripheral, central, or combined vestibular deficits [5, 7, 12-20]. Motion detection thresholds have also been studied [21]. There are two studies on SVV [22, 23]. Increased intra-individual variability in the deviations of SVV in patients with migraine and tension-type headache has been reported in the first study [22]. In the second study, deviations recorded in migraine patients were similar with the results of the healthy controls [23]. The purpose of our study was to investigate the SVV tilt in patients with migraine and without vertigo and to compare them with the results of healthy controls and patients with tension-type headache by using an inexpensive bedside test. Caloric tests and cVEMPs were also studied to find out if there was a correlation between these tests and the deviation of SVV.

MATERIALS and METHODS
The study was conducted in the specialized Neuro-otology Clinic in the department of Neurology, Ege University Faculty of Medicine, Izmir, Turkey. The study protocol was approved by the local ethics committee (Ethics Committee of Ege University Medical
Patients were recruited between July 2010 and December 2011. Informed consent was obtained from all the participants.

Based on the criteria of the International Classification of Headache Disorders, 2nd edition (ICHD-II 2004) [24], 20 patients with migraine without aura (MoA) (17 female and 3 male, mean age 32.7±8.5 years, mean disease duration 11.4±10.5 years) and 20 patients with tension-type headache (TTH) (18 female and 2 male, mean age 37.9±11.3 years, mean disease duration 9.6±7.3 years) were recruited; 24 other patients (23 female and 1 male, mean age 36.1±9.2, mean disease duration 12.2±7.8 years), diagnosed as definite vestibular migraine (VM) according to the criteria defined by Neuhauser et al. [25], constituted the third group of the study. In all VM patients, vertigo attacks were characterized by spinning of the environment or of the patients themselves. In 14 patients, vertigo attacks preceded the headaches; in 4, they occurred after the headache; and in 6, they were reported to start simultaneously. In 9 patients, vertigo attacks not temporally associated with headache were also present in addition to the attacks associated with headache. None of the patients described auditory symptoms during these vertiginous episodes. Headache was generally hemicranial in 19 and holocranial in 5 patients.

The neurological examination of all the patients with MoA, TTH, and VM was normal. None of them was using a preventive drug for at least a month, and the recordings were performed during the interictal period. The time interval from the last attack to the vestibular tests was 9.5±4.5 days in patients with MoA, 4.3±2.3 days in patients with TTH, and 18.2±11.3 days in patients with VM.

Thirty healthy volunteers of comparable age and gender distribution (25 female, 5 male, mean age 32.8±8.3 years) without personal or family history of vestibular symptoms, migraine, or TTH were taken as the control group (one-way ANOVA test was used to compare age and chi²-test was used to compare genders between groups, revealing no significant difference, p>0.05).

We performed a detailed neurotological and ophthalmological examination on all patients and healthy controls, which included examination of stance and gait, examination of saccadic and pursuit eye movements, cover testing to detect vertical misalignment, positional tests consisting of the Dix-Hallpike and roll maneuvers, and fundus examination. Pure tone audiometry, caloric tests, cVEMPs, and measurement of SVV deviation were the tests performed.

The ICS air caloric stimulator model NCA-200 (ICS, Schaumburg, IL, USA) was used for caloric tests with an air flow of 8 l/min at 25°C and 50°C within 60 s. Maximum slow phase velocity (SPV) was determined using the ICS velocity computer system. Caloric testing was evaluated for side difference (a 25% difference being considered significant) and bilateral hypofunction (maximal SPV of nystagmus for cold plus warm caloric stimuli should not exceed 12°/s). cVEMPs were recorded by using a Synergy device (Medelec; Oxford Instruments Medical Inc, Oxford, UK). To record the surface EMG activity, an active electrode was placed on the upper half of the sternocleidomastoid muscle ipsilateral to the stimulation, with the reference electrode placed on the upper third of the sternum and the ground electrode on the middle of the forehead. Patients were seated on an armchair and were asked to turn their head contralaterally to the ear being tested to achieve maximal activation of the sternocleidomastoid. Two stimulation sequences consisting of 100 sound stimuli were given. The acoustic stimuli were clicks at an intensity of 100 dBnHL (normal hearing level) of 0.1-millisecond duration, delivered at a frequency of 5 Hz through a headphone unilaterally to each ear. The EMG signal was band-pass-filtered from 10 to 1000 Hz and averaged during a 100-millisecond interval. The initial positive/negative polarity of the waveform with peaks was termed p13 and n23 on the basis of the respective latencies. The latencies of peaks p13 and n23 and peak-to-peak amplitude of p13-n23 were measured. To achieve independence from the level of background activation, the amplitude of the cVEMPs was expressed as the ratio of peak-to-peak amplitude divided by a mean prestimulus rectified EMG measured during the recording [26]. In order to determine the interaural amplitude asymmetry of cVEMP responses, an asymmetry ratio (AR) was calculated by using the following formula: AR%: 100 (Al-As)/(Al+As), where Al and As are the larger and smaller amplitudes, respectively, obtained from stimulating each ear [27]. SVV deviation was measured by the bucket method that was validated by Zwergal et al. [4]. Patients sat upright and looked into a translucent plastic bucket, with their visual field completely covered by the rim of the bucket. On the bottom inside the bucket was a dark, straight, diametric line, and on the bottom outside, there was a perpendicular line originating from the center of a quadrant divided into degrees, with the zero line adjusted to the dark line inside. For measurement the examiner randomly rotated the bucket clockwise and counterclockwise and brought it back toward the zero degree position. Patients were asked to indicate the position when they estimated the inside bottom line to be vertical. The examiner read the displacement from the verticality in degrees from the outside scale. The procedure was repeated 10 times, and the mean SVV deviation was calculated for each subject. It was expressed as the deviation from gravitational vertical (0°) measured in degrees and was taken into consideration. Positive values indicated deviations of the line to the subject’s right of vertical and vice versa.

Statistical Analysis
Statistical Package for the Social Sciences (SPSS) 20 for Windows was used for the statistical analysis. Hypothesis tests were performed at an α: 0.05 significance level (meaning p<0.05 was accepted as significant). The Shapiro-Wilk test was performed to check if the data were normally distributed. As none of the parameters was normally distributed, nonparametric methods were used. Multiple-group analyses were performed by using the Kruskal-Wallis test. Mann-Whitney U-test was performed for comparisons among the groups. The correlation analysis between the SVV deviation, caloric tests, and VEMPs was studied by Spearman’s correlation test. Fisher’s exact test was used to test if an absolute SVV deviation greater than 2 degrees could be used to differentiate patients with migraine from healthy controls.

RESULTS
The neurotological and ophthalmological examination was normal in all patients, with no sign of head tilt, vertical misalignment, or ocular torsion that may indicate ocular tilt reaction.

None of the patients or controls had hearing loss on pure tone audiometry.
Caloric testing, performed in normal controls and patients with MoA and TTH, revealed neither an asymmetry between the right and the left ears nor bilateral paresis. On the other hand, in 5 of the 24 patients with VM (20.8%), a unilateral peripheral vestibular deficit (left-sided caloric paralysis in 1, left-sided paresis in 3, and a right-sided paresis in 1 patient) was found.

cVEMP latencies, p13-n23 amplitudes, and amplitude AR of patients with MoA, VM, and TTH were not statistically different from the results of the healthy controls (p>0.05).

Median SVV deviation values of the healthy controls and the patient groups are given in Table 1. When the values recorded from the healthy controls were compared with the values of the patients, no statistically significant difference could be found (p: 0.31) (Figure 1).

As a second step, individual results of the subjects were taken into consideration. As SVV tilts exceeding 2 degrees to either side is generally accepted as abnormal, subjects were searched for such a tilt. None of the controls or patients with TTH had tilts greater than 2 degrees. On the other hand, 3 patients with MoA (15%) and 3 (12.5%) patients with VM had tilts exceeding 2 degrees. Fisher’s exact test was used to see if an absolute SVV deviation greater than 2 degrees could be used to differentiate patients with migraine from healthy controls, with an insignificant result (p: 0.075).

Finally, we checked for the deviations exceeding 2 degrees for the 10 trials in SVV measurements in each subject to assess the intra-individual variability in the deviations of SVV (Figure 2a-d). Kruskal-Wallis test revealed a significant difference in intra-individual variability between the four groups (p:0.007). Mann-Whitney U-test was used for comparisons between patients with MoA and healthy controls, revealing a larger variability in patients with MoA (p: 0.007). The same was true for the patients with VM (p<0.001). However, the results of the patients with TTH were not different from the results of the control subjects (p: 0.2). The results of patients with MoA were not different from the results of patients with VM (p: 0.25).

To test an association between caloric tests, cVEMPs, and the SVV deviation, Spearman’s correlation test was performed. No significant correlation was present between the SVV deviation and the right- and left-sided VEMP latencies and amplitudes (p13 latency: right side r: -0.72, p: 0.57, left side r: -0.21; p: 0.08, n23 latency: right side r: -0.15; p: 0.22, left side r: -0.79; p: 0.53, right p13-n23 amplitude: r: -0.028; p: 0.82, left p13-n23 amplitude: r: -0.038; p: 0.76).

No correlation between the right-and left-sided caloric test results and the SVV deviation was found (right side r: -0.18; p: 0.85, left side r: 0.15; p: 0.17). When taken individually, there were 5 patients with VM having unilateral caloric paresis or paralysis. The one with left-sided paralysis had a 2-degree tilt of the SVV to the same side. On the other hand, the patient with a left-sided paresis had a 5-degree tilt of the SVV to the left side, and the other one with a right-sided paresis had a 4-degree tilt to the right side. One of the two other patients with a left-sided paresis had no tilt (0 degrees), and the other had a 2-degree tilt to the right side. None of the three patients with MoA with SVV tilts exceeding 2 degrees had any caloric test abnormality.

**DISCUSSION**

Perception of verticality depends on the integration of vestibular, visual, and somatosensory information [28, 29]. Lesions involving the central integrating system or central or peripheral vestibular system can lead to abnormal perception of body orientation in space and

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**Table 1. Deviation of the SVV (deg) in healthy controls and in patients with MoA, VM and TTH**

<table>
<thead>
<tr>
<th>Group</th>
<th>SVV (deg)</th>
<th>p: 0.31</th>
</tr>
</thead>
<tbody>
<tr>
<td>MoA</td>
<td>med: 1</td>
<td>min: -3.5</td>
</tr>
<tr>
<td>VM</td>
<td>med: 0.75</td>
<td>min: -5</td>
</tr>
<tr>
<td>TTH</td>
<td>med: 1</td>
<td>min: 0</td>
</tr>
<tr>
<td>Controls</td>
<td>med: 0</td>
<td>min: -2</td>
</tr>
</tbody>
</table>

SVV: subjective visual vertical; MoA: migraine without aura; VM: vestibular migraine; TTH: tension type headache; p: significance value (comparison of the patient groups with the healthy controls)
abnormal perception of vertical \[^1\]. Recent studies have shown that awareness of the body orientation may also modulate verticality representation, indicating the importance of the cognitive systems \[^30\]. Significantly more patients with migraine have vertigo compared to patients with TTH and headache-free controls \[^5\]. Vestibular dysfunction beginning from the labyrinth to the cerebral cortex due to migraine mechanisms has been proposed as an explanation \[^7, 8\]. Migraine patients with vertigo have been reported to have a 20%-25% prevalence of caloric hypofunction, indicating involvement of the horizontal semicircular canals \[^5, 7, 15\]. cVEMP abnormalities, including absent or delayed cVEMPs \[^16, 17\] or cVEMPs of normal latency but reduced amplitude, have been reported in different studies \[^18\], which were proposed to indicate lesions of the sacculocollic pathways in the brainstem or saccular damage. On the other hand, in the two latest studies, cVEMPs of normal latency and amplitude have been reported in patients with VM \[^19, 20\].

Motion detection thresholds have also been studied in patients with migraine, and a dramatic threshold reduction has been reported in VM compared to normal and migraine subjects, especially for head motions modulating canal and otolith inputs together, which was ascribed to changes in the canal-otolith integration in the brain \[^21\].

SVV deviation in patients with migraine has been studied by two groups \[^22, 23\]. In both of these studies, a potentiometer has been used to adjust the line to the gravitational vertical, measured with a precision of 0.1 degrees. By this method, Asai et al. \[^22\] have found larger deviations both in patients with migraine and TTH when compared with patients without headache. However, the average deviations of the SVV in both groups of patients with primary headache were within the normal range obtained in healthy subjects. An important finding was that approximately 65% of patients with primary headache showed more than 2 degrees of tilt at least once in eight trials performed during the study. The figure was 18% for the patients without
headache. Intra-individual variability in the deviations of SVV was significantly larger in patients with migraine and TTH when compared with patients without headache. The authors also performed caloric testing, cVEMP, and static posturography, without a significant difference between the three groups studied. They concluded that patients affected by migraine or TTH may have a subclinical abnormality of the SVV, resulting in the occurrence of subjective imbalance \[22\]. In the other study performed by Crevits et al. \[23\], SVV deviations of migraine patients were compared with deviations recorded in healthy controls, revealing no significant difference between the two groups.

In our study, patients with MoA and TTH did not show any abnormality on caloric testing. On the other hand, 5 of the 24 VM patients (20.8%) showed unilateral caloric paresis or paralysis consistent with the previous results \[5, 7, 15\]. None of the patient groups showed any cVEMP abnormality. cVEMP were recorded in all the patients tested, from both sides, with p13 and n23 latencies not different from the healthy controls. The same was true for both sided p13-n23 amplitudes \[20\].

The median SVV deviation of our patient groups was not different from the deviation recorded in healthy controls. When a tilt greater than 2 degrees to either side was taken into consideration, it was found that 15% of patients with MoA and 12.5% of patients with VM had tilts greater than 2 degrees, whereas tilts in healthy controls and patients with TTH were below this level. However, the statistical analyses showed that SVV tilts exceeding 2 degrees could not be used to differentiate patients with migraine from the healthy controls. Despite not having differences in the median SVV deviation compared to controls, patients with migraine, either associated with vertigo or not, had significantly larger variability in their SVV measurements when all 10 of their trials were taken into consideration (Figure 2 a-d). Larger intra-individual variances were similar with the study of Asai et al. \[22\]. They reported the same finding in their patients with TTH \[22\]. However, our TTH patients revealed normal results. Our finding seems to be consistent with previous clinical studies reporting that the prevalence of vestibular symptoms and signs in TTH is similar to that in the general population \[30\].

We could not find a correlation between the caloric tests, cVEMP, and the SVV deviation. Caloric tests check the activity of the horizontal semicircular canals, and cVEMP check the activity of the sacculus, whereas SVV deviation is thought to be mainly utriculus-related. As different parts of the labyrinth and its central connections are investigated by these tests, inexistence of a correlation between them seems quite logical.

The comorbid aspects of balance, migraine, and anxiety disorders are viewed as the product of sensorimotor, interoceptive, and cognitive adaptations that are produced by afferent interoceptive information processing. A vestibulo-parabrachial nucleus network, a cerebral cortical network (including the insula, orbitofrontal cortex, prefrontal cortex, and anterior cingulate cortex), a raphe-nuclear vestibular network, a coeruleo-vestibular network, and a raphe–locus coeruleus loop \[81\]. We have also learned from recent studies that awareness of body orientation is also important in modulating verticality representation, which supports the importance of cognitive systems \[80\].

Average SVV deviation of our patients either with migraine or TTH was not different from the controls. The only difference was the larger variability of the SVV measurements during the 10 trials recorded in patients with migraine either associated with vertigo or not. It is difficult to interpret this vague finding as a dysfunction of the graviceptive pathways. A more plausible explanation can be the operation of cognitive processes causing defective perception of verticality.

Though the method we used in our study is not as precise as the method used in previous studies, our results are not very different from the results gathered by using more sophisticated methods. The bucket method seems to be a reliable procedure to study SVV. As it is an inexpensive and simple bedside test, it can be used in every clinic. Further studies are needed to support both its reliability and our findings in migraine patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ege University Faculty of Medicine, reference number 10-5/21, approval date June 10th, 2010.

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

Peer-review: Externally peer-reviewed.


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

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