Interaural Difference Values of Vestibular Evoked Myogenic Potential in Migraine Patients

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Abstract- Migraine is a neurologic disease, which often is associated with a unilateral headache. Vestibular abnormalities are common in migraine. Vestibular evoked myogenic potentials (VEMPs) assess otolith function in particular functional integrity of the saccule and the inferior vestibular nerve. We used VEMP to evaluate if the migraine headache can affect VEMP asymmetry parameters. A total of 25 patients with migraine (22 females and 3 males) who were diagnosed according to the criteria of IHS-1988 were enrolled in this cross-sectional study. Control group consisted of 26 healthy participants (18 female and 8 male), without neurotological symptoms and history of migraine. The short tone burst (95 dB nHL, 500 Hz) was presented to ears. VEMP was recorded with surface electromyography over the contracted ipsilateral sternocleidomastoid (SCM) muscle. Although current results showed that the amplitude ratio is greater in migraine patients than normal group, there was no statistical difference between two groups in mean asymmetry parameters of VEMP. Asymmetry measurements in vestibular evoked myogenic potentials probably are not indicators of unilateral deficient in saccular pathways of migraine patients.

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Keywords: Migraine; Vestibular evoked myogenic potential; Vestibular asymmetry; Laterality of headache

Introduction

Migraine is a common neurologic syndrome associated with altered function of some brain pathways. A migraine headache is typically unilateral. It is suggested that unilateral pain results from an asymmetrical brainstem dysfunction (1).

Some migraine patients with and without vestibular symptoms may have abnormal vestibular test results (2, 3). In migraine patients, it is important to examine the symmetry of vestibular function in electrophysiologic evaluations to rule out an asymmetric function indicative of a lateralized vestibular lesion.

Vestibular evoked myogenic potential (VEMP) is one evaluation to assess the symmetry of saccular function (4). VEMPs, recorded from the contracted sternocleidomastoid muscle (SCM), are inhibitory potentials resulting from ipsilateral loud acoustic stimulation (5-10). They have a short-latency reflex passing in the brainstem. The latency of its components implies a rapidly conducting oligosynaptic pathway that include the saccule, inferior vestibular nerve and vestibular nuclei as afferent parts as well as the vestibulospinal tract, accessory nucleus and its derivations to the SCM as efferent parts (11-14). Moreover, abnormal VEMPs may be caused by brainstem lesions. There are several reports of VEMP abnormalities in diseases of the brainstem (11).

There are few analyses of VEMP in migraine patients. One study on patients with basilar artery migraine has reported no VEMP or delayed VEMPs. Liao and Young (2004) in this study assessed the role of VEMP in monitoring basilar migraine patients with no or delayed VEMPs following preventive therapy. The authors reported that abnormal VEMPs may be due to interrupted descending saccular pathways in the

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brainstem (15). Allena and Roceana (2007) reported deficit of habituation and reduced amplitudes in migraine patients, which suggested reduced serotonergic control of VEMP pathways. Bier *et al*., (2009) also noted reduced VEMP amplitudes in vestibular migraine patients. They concluded that both peripheral and central vestibular structures are affected in this disease (2,16). The above studies, however, did not assess the interaural differences of VEMP. Object of the present study is to assess interside difference values of VEMP in patients with migraine compared to normal participants. Furthermore, we compared the same parameters between two groups of patients with unilateral and bilateral headaches to investigate the influence of headache laterality on VEMP parameters.

Materials and Methods

A total of 25 (22 female, 3 male) patients with migraine diagnosed according to the International Headache Classification (IHS-1988) criteria were enrolled in this cross-sectional study. Magnetic Resonance Imaging (MRI) and physical examinations ruled out other neurologic problems. The control group consisted of 26 healthy participants (18 female, 8 male) with no neuro-otological symptoms, history of migraine or any other type of headaches. All participants entered the study after obtaining informed consent.

All patients took no prophylactic medications for at least three months. Patients' ages were between 21- 51 years (37.42 ± 8.56) and the age range in the control group was 20- 53 years (32.67 ± 9.27). The study excluded all participants with neck problems and history of vestibular diseases. All participants underwent a basic audiological evaluation including pure tone audiometry (250–8000 Hz), tympanometry and acoustic reflex test to rule out any possible conductive component of hearing loss.

Patients underwent VEMP testing when they were headache-free (at least 24 hours following the latest attack). The test was performed with an auditory evoked potential apparatus (ICS CHARTR EP, GN otometrics, United States.) equipped with PA-800 preamplifier. The active electrodes were placed over the middle of each SCM with a reference electrode on the upper end of the sternum and ground electrode over the forehead. Short tone bursts of 500 Hz with 2 ms rise/fall times and plateau 0 ms with stimulation rate of 5.1/sec presented to the ear ipsilateral to the contracted SCM muscle through the insert earphone (ER-3A). Stimulus intensity was 95 dB. Analysis time for each stimulus was 100 ms. Responses up to 150 stimuli were averaged for each test and band-pass filtered from 10-1500 Hz (17). Two consecutive runs performed on the same ear to check reproducibility.

VEMP testing was performed in a sitting position. During VEMP recording, participants were instructed to flex their heads forward by about 30°, and then 80° opposite from the stimulated ear to activate the ipsilateral SCM. To monitor muscle contractions during VEMP, a feedback method using a blood pressure manometer with an inflatable cuff was applied. The cuff was inflated to a standard pressure of 20 mm Hg, and then an audiologist helped participants to place the cuff between their hand and jaw. Once in position, participants pressed with their chins against the hand-held cuff to reach a cuff pressure of 40 mm Hg (2,18,19). Furthermore, we instructed subjects to fix their eyesight to the 40 mm Hg figure in the manometer as changes in eye position may affect amplitude of the response (20).

To determine interaural differences in participants, we calculated the side difference of amplitudes, latency of p13, n23 and interpeak latencies (IPL) and side difference of VEMP threshold. For computing side-differences, we subtracted the right and left values for all parameters in all participants, and then compared the mean of this difference between normal and migraine groups, and between patients with unilateral and bilateral headaches.

Amplitude ratios were calculated as the difference of p13-n23 amplitude in the right and left ears divided by the sum of p13-n23 amplitudes of both ears. To compare groups in terms of the side difference values, we used the independent t-test. For same comparison between patients with and without unilateral headaches, the Mann-Whitney U test was used. Right and left side values were compared using paired t-test. SPSS statistical software performed statistical analyses. A P.value < 0.05 was considered statistically significant.

Results

We classified current patients according to migraine symptoms such as duration of affection, side of headache, number of attacks in one month, associated symptoms, existence of aura and vertigo, effect on daily activity, family history and intensity of pain according to the Visual Analog Scale (VAS) scale (Table 1).

VEMP responses were recorded in all participants. Figure 1 presents an example of VEMPs obtained in both groups.

In the normal group, the mean (± SD) interside differences of p13, n23 and IPL latencies were 0.73 ms (±0.58), 1.00 ms (±0.69) and 0.98 ms (± 0.74), respectively. In the migraine group, the mean interside difference of p13, n23 and IPL latencies were 1.16 ms (± 1.32), 1.08 ms (± 0.65) and 1.14 ms (± 0.90), respectively. Independent t-test showed no significant statistical differences between the two groups (*P*=0.13 for p13, *P*=0.67 for n23 and *P*=0.50 for IPL).

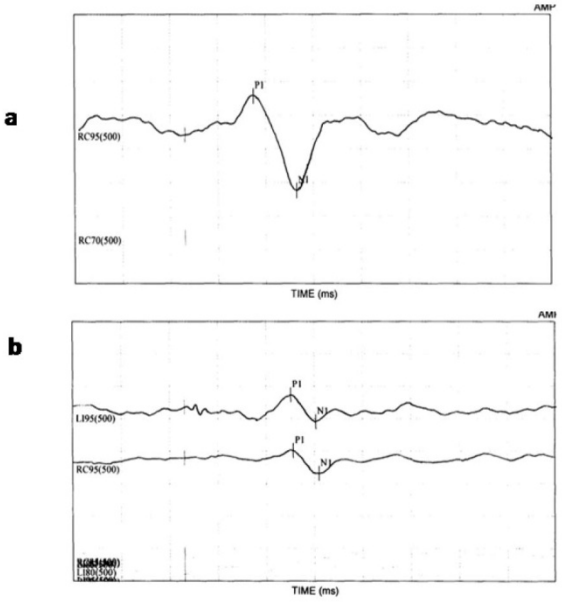

Figure 1. VEMP response in (a)
a normal subject and (b) a migraine patient

Table 1.Characteristics of a migraine headache

Characteristic		Number	Percent
Length of affection	**≤5 years**	8	32%
	Between 5-10 years	7	28%
	>10 years	10	40%
Frequency of attacks	**3 ≤**	15	60%
	>3	10	40%
Vertigo	+	12	48%
	_	13	52%
Aura	+	4	16%
	_	21	84%
Accompanying symptoms	**Photophobia**	12	48%
	phonophobia	21	84%
	Nausea	19	76%
	Vomiting	13	52%
Family history	+	20	80%
	_	5	20%
Laterality	**Unilateral (often)**	17	68%
	Bilateral (often)	8	32%
VAS (Visual analogue scale)	**>5**	23	98%
	<5	2	2%

The mean interside differences in amplitude and threshold were 37.30μv (± 36.15) and 3.40 μv (± 3.23), in the healthy group. While the mean interside differences in amplitude and threshold were 28.41μv (± 19.68,) and 2.70μv (± 2.94), in patients with migraine. Statistical analysis by independent t-test did not show significant differences between the migraine and control groups in these parameters (*P*=0.28 for amplitude and *P*=0.44 for threshold).

In both groups, the amplitude ratio was computed to

compare right and left side values. The mean amplitude ratio was 0.08μv (± 0.07) in the control group and 1.14μv (±0.90) in patients with migraine. The two groups had no statistical difference in terms of amplitude ratios (*P*=0.14).

In two groups of patients, those with unilateral and bilateral headaches, the mean interside difference of VEMP parameters was compared, which showed no significant statistical association (Tables 2,3).

Table 2. Interside differences of latencies (mean±SD) on VEMP between migraine patients with unilateral (n=17) and bilateral (n=8) headaches

	IPL	n23	p13
Unilateral	1.16±1.32	1.10±0.66	1.07±0.94
Bilateral	1.17±1.23	1.04±0.68	1.29±0.85
Mann-Whitney	0.97	0.76	0.41

Table 3. Interside differences of amplitude, threshold and amplitude ratio (mean±SD) on VEMP between migraine patients with unilateral (n=17) and bilateral (n=8) headaches

	Amplitude	Threshold	Amplitude ratio
Unilateral	26.51±21.01	2.64±3.12	0.09±0.07
Bilateral	32.47±17.06	2.85±2.67	0.17±0.15
Mann-Whitney	0.52	0.77	0.10

Discussion

In electrophysiologic measurements such as VEMP, symmetry of results between both ears is important; lack of this symmetry could be a sign of a unilateral deficit in the vestibular system. One of the overall goals of VEMP analysis is to assess symmetry of saccular function by comparing the right versus left sides (21). Unilateral pain is a typical symptom in migraine patients (1) that potentially may affect VEMP interside difference values. This study assessed this probability.

According to the literature, interside latency differences greater than 3.5 ms are considered abnormal. Also, VEMP thresholds should be within 10 dB of each other to be normal. Amplitude ratios vary among studies but generally amplitude ratios over 0.34 or 0.35 for adult subjects less than 60 years of age are considered abnormal (9,21-25).

In the present study, there were no significant differences between migraine and normal groups in terms of the amplitude ratio and interside difference values. A comparison of right and left values in the migraine group (paired t-test) also showed no difference between the two sides. Comparison of results between the two groups of patients with unilateral and bilateral headaches also did not show statistical differences in terms of the amplitude ratio and interside difference values.

Although in this study there was no significant difference between the two groups, however in one patient the amplitude ratio was greater than the normal range. This patient had more frequent unilateral headaches per month than other patients. In another patient, the interside difference for p13 was abnormal (more than 3.5 ms). The duration of her disease was over 25 years, and she was among the most affected patients who had over five attacks in one month. Her VAS score without psycholeptic drugs was almost 10, but her headaches were not always unilateral.

It is shown in one study that spasm of the vestibular branch of the internal auditory artery may result in ischemic damage of the vestibular labyrinth, which gives an asymmetric caloric test response (i.e., unilateral canal paresis or directional preponderance (15). Thus, spasm in the vestibular branch of the internal auditory artery probably may affect the saccule, causing an asymmetry in the VEMP response.

Histopathological findings in one study suggested that sudden left-sided deafness in one patient with left-sided headache resulted from ischemia. The ischemia was most likely due to migraine-associated vasospasm. Although the damage was restricted to the cochlea, and the left saccule was normal, however saccular involvement could occur (25,26).

Current findings did not show unilateral complications of migraine headaches. The study patients with unilateral headache did not always have headaches only in one side, and the affected side sometimes changed alternatively in attack periods. Attack was often (not always) unilateral for unilateral patients and often bilateral for bilateral patients. The lack of consistency

regarding the location of the headache and low sample size are possible reasons that amplitude ratio and side difference values were not statistically different between the migraine and control groups.

Various studies have assessed blood flow changes in different migraine phases. These studies have shown that cerebral oligemia and hyperemia are not always in the same region of the symptoms and not limited to the side of the headache.

In other words, even in unilateral headaches all brain regions and not only the side of the headache are subject to vascular changes (26, 27). An MRI study also did not discuss laterality and interside differences in migraine patients. But findings of a PET study have suggested that lateralization of pain in migraines was due to asymmetrical brainstem dysfunction (1). Weiller *et al*., reported that brainstem activation during a migraine attack in patients with no aura had slightly more dominance contralateral to the side of the headache (27). However, clinical manifestation of this finding was not observed in current VEMP analysis.

Patients in the present study differed from each other in terms of frequency of attacks per month, time of last attack and duration of affection. Therefore, it is better to conduct this study in a more homogenous group of patients. Another limitation of this study is the lack of visual monitoring of EMG activity during the test. Although Vanspauwen et al. reported usefulness of blood pressure cuff in monitoring of SCM muscle contraction; it could be controlled ideally by visual control of the EMG level during the test (19).

In conclusion, the diagnostic value of VEMP asymmetry measurements in migraine patients is not high because there is no meaningful difference between migraine patients compared with a healthy group in the VEMP asymmetry measures. Furthermore, unilateral headaches in migraine patients do not result in abnormalities in VEMP side difference measures. The low number of patients with pure unilateral headache in the present study suggests the need for conducting additional researches with more cases.

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