VESTIBULAR EVOKED MYOGENIC POTENTIAL

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Introduction

Vestibular evoked myogenic potentials are neurophysiological method for examining of saccular function, the bottom of the vestibular nerve that in nerves the sacculus and central vestibular pathways. Those are inhibitory potentials of the saccule and utriculus; Vestibular Diseases; Vestibular Function Tests; Male; Female

Material and methods.

This research was meant to be a prospective study which included 30 normal audiovestibular volunteers of both sexes. The group consisted of 53.3% women and 46.7% men. The saccular function testing by vestibular evoked myogenic potentials was performed monaurally using air-conductive 500 Hz tone burst auditory stimulation. Results.

The average value of the p13 wave latency in healthy subjects of this study was 15.18 ms (±1.24) while the mean latency of n23 waves in the same subjects was 25.00 ms (±2.23). The average value of the amplitude of the p13-n23 waves was 80.28 (±0.4) microvolts. Conclusion. The difference in the values of the basic parameters of vestibular evoked myogenic potential responses between men and women does not exist. No differences between the right and the left ear in the values of latency and amplitude were observed. Key words: Vestibular Evoked Myogenic Potentials; Vertigo; Sacculle and Utricle; Vestibular Diseases; Vestibular Function Tests; Male; Female

Summary

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Sažetak

Uvod. Vestibularno evocirani miogeni potencijali predstavljaju neurofiziološku metodu za ispitivanje funkcije sakulusa, donjeg vestibularnog nerva koji inerviše sakulus i centralnih vestibularnih puteva. Oni su inhibitori potencijali saccule i utrikuli, koji rezultiraju odgovorom na ipsilateralnu akustičku stimulaciju sakulusa. Parametri testa vestibularno evociranog miogenog potencijala su prag latencije p13 i n23 talasa i interamplitude p1-n1, interauralna razlika p13 i n23 latencije i razlika u amplitudama izmedju oba uva. Cilj ove studije bio je da se učinak standardizacija parametara vestibularno evociranog miogenog potencijala odgovora, latencija p13 i n23 talasa, amplituda odgovora i interauralna razlika u amplitudi odgovora i da se utvrdi da li postoji razlika u vrednostima izmedju polova. Materijal i metode. Istraživanje je načinjeno kao prospektivna studija kojom je obuhvaćeno 30 audiovestibularno zdravih dobrovoljaca, oba pola. Grupu je činilo 53,3% žena i 46,7% muškaraca. Ispitivanje funkcije sakulusa vestibularno evociranim miogenim potencijalima vršeno je unila
teralno, vazdušno provođenjem, tone burst 500 Hz zvučnom stimulacijom. Rezultati. Prosječna vrednost latencije p13 talasa kod zdravih ispitanika u ovoj studiji bila je 15,18 ms (±1,24), a srednja vrednost latencije n23 talasa kod njih iznosila je 25 ms (±2,23). Prosječna vrednost latencije amplitude p13-n23 talasa bila je 80,28 (±0,4) mikrovoltoa. Zaključak. Razlika u vrednostima osnovnih parametara vestibularno evociranog miogenog potencijala odgovora izmedju muškaraca i žena ne postoji. Nije konstatovana razlika ni izmedju desnog i levoj uva u vrednostima latencija i amplitude kod oba pola. Ključne reči: Vestibularni evocirani miogeni potencijali; Vertigo; Sakulus i utrikulus; Vestibularna oboljenja; Testovi vestibularne funkcije; Muško; Žensko

Reference
At that time, measurement of sound evoked potentials was not found clinically applicable. It was after the pioneering work of Colebatch, Halmagy, and Skuse in 1994 that the measurement procedure of myogenic potentials evoked by a click started to be applied. These authors introduced the technique of measuring vestibular evoked myogenic potentials by placing electrodes not on the back of the head but over the sternocleidomastoid muscle. By using high quality electromyographic measurement techniques, they documented the response that could be reproduced. This response was described as a “click evoked vestibulo-colic response” that was later renamed vestibular evoked myogenic potentials (muscle potentials originating from stimulation of the vestibular organ) and that term is used today [3].

Vestibular evoked myogenic potentials (VEMP) are exclusive to the evaluation of otoneurologic patients. VEMP are the inhibitory potentials of the sternocleidomastoid muscle in response to ipsilateral acoustic stimulation of the sacculus.

The aim of recording vestibular evoked muscle potentials is to determine whether there is a normal function of the sacculus, lower vestibular nerve that innervates the sacculus, and central vestibular pathways. The sacculus, a lower part of otoletic organs, has a certain sensitivity to sound that can be measured by recording the muscle potential. The sensitivity to the sound of the sacculus is believed to represent the rest of its functions as a hearing organ in the lower animals. A reflexive way responsible for causing the potentials originates from the sacculus, which is stimulated by the sound intensity. The action potentials from the sacculus are transmitted through a lower vestibular nerve to the lateral vestibular nucleus. From here, impulses proceed through the medial vestibulospinal tract (MVST) towards the accessory nucleus and further on towards the ipsilateral sternocleidomastoid muscle. VEMP response consists of an initial positive wave (p13) followed by a negative wave (n23) (figures 1 and 2). The following components with a lower stimulus threshold are not of vestibular origin [1–5]. Having in mind that peripheral and central pathways are activated in the vestibular evoked potentials, abnormal VEMP findings are recorded with lesions in any part of these structures. Sound that stimulates the sacculus and causes VEMP should be transmitted to the sacculus, which means that the middle ear should be intact. Vestibular evoked myogenic potentials mainly test the lower part of the brain stem while auditory evoked brain stem potentials provide data about the rostral part of the brain stem.

### Material and Methods

The study was made at the Department for Audio and Vestibulology, the Department of Ear, Nose and Throat Diseases of the Clinical Center of Vojvodina in Novi Sad, as a prospective study that included 30 healthy subjects of both sexes.

Upon obtaining the anamnesis, an otoscopic examination was made. The subjects with pathological findings during otoscopy and tympanometry were excluded from the study. Hearing threshold was determined by tonal liminar audiometry.

The saccular function was tested by vestibular evoked myogenic potentials (VEMP). VEMP measuring was performed by placing the electromyography (EMG) electrodes in the middle third of m. sternocleidomastoides of a patient in the sitting position with the head turned to the side trying to touch the shoulder with the chin, thus allowing maximum contraction of m. sternocleidomastoides without any activity of the neck muscles without VEMP. The reference electrode

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**Abbreviations**

- VEMP – vestibular evoked myogenic potential
- ms – milisecond
- μV – microvolt
- dBnHL – decibel above normal adult hearing level
- SCDS – semicircular canal dehiscence
- MVST – medial vestibulospinal tract

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**Figure 1.** Normal finding of VEMP response on both sides

**Figure 2.** Normal response on the left side, no answer on the right side

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**Slika 1.** Uredan nalaz vestibularno evociranog miogenic-nog potencijala

**Slika 2.** Normalan nalaz levo, bez odgovora na desnjoj strani
was placed on the sternum and the ground one to the forehead.

Stimulation was conducted via the headphones by click-stimuli or burst-tones monaurally. Clicks, usually of 95-100 dBnHL intensity, were presented to each ear every 200 ms, a total of 200. Optimal frequency for tone-burst was 500 Hz and 5 stimuli were presented per second. VEMP responses were amplified, filtered, and the mean value of at least 100 presentations was calculated and then displayed on the monitor (Madsen Capella). Furthermore, the latency, amplitude of waves p13-n23 were measured, and their threshold determined. Due to the high intensity of the stimulus, the headphones had to be calibrated. In order to ensure that VEMP responses were reproductive, two repeated tests were made. Generally, VEMP was easily obtained since the potentials were robust. Sound evoked VEMP were almost entirely unilateral.

Results

The study included 30 healthy volunteers. The group consisted of 53.3% women and 46.7% men. The average age was 34.4 years (the youngest subject was 18 and the oldest was 57 years old). The average age of male subjects was 38.43 years, while women were slightly younger; their average age being 30.88 years.

Normal otoscopic findings and tympanometry curve of type A were observed in all patients. All subjects had normal hearing threshold (up to 20 dBnHL).

Analysis of VEMP Responses

For clinical interpretation of vestibular evoked myogenic potentials, the most important parameter was the latency of waves p13 and n23. In addition, the response amplitude and interaural difference were observed. The average value of p13 wave latency in healthy subjects was 15.18 (±1.24) ms (males 15.25 (± 1.71) ms, females 15.12 (±1.14) ms) (Graph 1), and the mean latency of n23 waves was 25.00 (± 2.23) ms (males 25.18 (± 3.1) ms, females 24.83 (±2.46) ms) (Graph 2). The average amplitude value of p1-n23 wave was 80.28
The mean value of p13 wave latency of the right ear was 15.25 ms (±1.62). Similar values of p13 waves latency were observed in both sexes, 15.24 ms (±1.09) in males and 15.28 ms (±2.01) in females. There was no statistically significant difference in the measured values of the latency between men and women on the right ear (r = 0.012, p>0.05).

When analyzing the mean value of p13 latency for the left ear expressed in ms it was found to be 15.10 (± 1.1) ms. Slightly higher values were observed in men 15.26 ms (± 0.7) compared with women 14.95 ms (±1.37), but with no significantly statistical difference (r = -0.142, p> 0.05).

The average n23 wave latency of the right ear was 24.75 ms (± 2.93). The mean values for this parameter of 25.3 ms were in men (± 3.61) and 24.26 ms (± 3.61) in women. Statistical analysis showed no significant difference in the correlation between the sexes (r = -0.181, p> 0.05).

Approximately the same n23 waves latency was described for the left ear of 25.25 ms (±1.98), in males 25.07 (±2.59) and females 25.41 (±1.31).

There was no statistically significant difference between the sexes in the values of n23 waves latency to the left ear (r = 0.087, p> 0.05).

The p13-n23 wave amplitude of the right ear was 83.85 μV (±38.37). A slightly larger amplitude was recorded in women 87.56 μV (±44.59) compared with men 79.85 μV (±44.59). There was no statistically significant difference between the sexes in the values of P13 amplitude waves in the right ear (r = 0.099, p> 0.05).

The p13-n23 wave amplitude of the left ear was 76.7 μV (±34.112). In this case, there was a slightly higher amplitude in women, being 78.57 μV (±29.49) compared with men, being 74.57 μV (±39.78). There was no statistically significant difference between the sexes in the values of p13 amplitudes waves in the left ear (r = 0.060, p> 0.05).

The difference in the amplitude values between the two ears is considered pathological if its value is over 0.36. It is calculated by the formula: AR%=100*(A_L-A_R)/(A_L+A_R) where A_L and A_R is the maximum and minimum amplitude of the observed ear.

The average difference in the amplitudes between the two sides was 0.17, 0.18 in men and 0.16 in women.

Discussion

Since VEMP test had been introduced as a new diagnostic method in audiology at the Department of Ear, Nose and Throat Diseases and used on patients with vestibular disorders, the aim of this study was to compile standardization of parameters of VEMP responses and to compare them with experience published in literature. The study subjects were healthy volunteers with normal hearing of both sexes. The group consisted of 14 (46.7%) men and 16 (53.3%) women, their average age being 34.4 years (ranging from 18 to 57 years). The subjects had no changes in hearing and denied the existence of other diseases. The standardization of values of VEMP responses was made. In order to interpret the findings accurately, the subjects had to have their hearing threshold in the normal/physiological range. Tympanometry curve was of type A in all subjects. Normal function of the middle ear was a prerequisite for further examination.

The mean value of hearing determined by tonal audiometry in 30 patients was within the normal values (up to 20 dBnHL) and by frequencies it was 500, 1000, 2000 and 4000 Hz respectively 6.26, 7.25, 8.25 and 9.48 dBnHL.

Vestibular evoked myogenic potentials are a neurophysiological method for examining the function of the saccus and the integrity of the lower vestibular nerve. VEMP are ipsilateral inhibitory myogenic potentials caused by the impact of high intensive transient acoustic stimuli.

VEMP procedure is recommended to be done in sitting or lying position with the patient’s head turned towards the opposite ear to allow maximum tension of the sternocleidomastoid muscle on the test side in order to place the electrode in the middle third of the muscle. The reference electrode was placed on the forehead and the grounding one on the sternum. Li recommends placing the reference electrode on the wrist [4]. A problem arises if there is no cooperation with the patient and he fails to achieve muscle tone tension, and in that case, it is impossible to conduct measurements. There are difficulties in performing the test with children, depending on their age. Aloud click or tone burst (recommended intensity of 95 and 100 dBnHL) in the interval of 200 ms (5/second) should be used for response stimulation.

Many authors agree that approximately the same answer is received no matter what kind of sound stimulation we used for [5, 6]. However, the advantage is given to the tone burst stimulation compared to a click (since it uses a lower intensity of absolute stimulation). Rauch et al. recommend tone bursts and the frequency of 500 Hz as the optimal stimulus [7]. The recommended stimulation parameters and frequencies were used in this study.

Stimulation can be unilateral or bilateral. Binaural measurement is faster but it is more accurate to perform unilateral measurement since there is a possibility of “transferring” response to the affected side when the test is done simultaneously stimulating both ears [8].

A high-intensity sound is needed as a stimulus in order to create VEMP response and it is necessary to check the position of headphones in the external auditory canal. The slightest mistake in terms of malposition or removing of headphones may result in the loss of VEMP response and poor
clinical interpretation due to sound intensity reduction.

In order to check the reproducibility of response or lack of it, it is necessary to make at least two measurements.

Measuring VEMP by bone conduction when using tone burst (through the forehead or lateral part of the skull, at frequency of 200 Hz) induces a significantly stronger VEMP test stimulus and does not lateralize as well as the tone click [10]. Galvanic stimulation can also cause VEMP response [9]. Stimulation by this technique is primarily used to differentiate lesions of the saccule, lower vestibular nerve and proximal nerve lesions. This technique requires special methodology due to a large number of electrical artifacts created by the stimulation. With galvanic stimulation of the vestibular nerve, it is expected that VEMP response is less sensitive with partial lesions of the vestibular nerve (vestibular nerve section) and that there is no response in a complete loss of function of the vestibular nerve. For this reason, galvanic stimulation cannot differentiate between the damage of the sacculus and lower vestibular nerve since the galvanic VEMP is expected to produce a response even when there is a damage of the lower vestibular nerve. Galvanic VEMP may be more reliable than the acoustic VEMP for methods of monitoring vestibulospinal connections through the spinal cord [11]. It is obvious that this method requires more research.

The following is observed in VEMP responses: how they are formed by sides, p13 and n23 latency, amplitude response and interaural difference.

VEMP response consists of a biphasic wave with an initial positive or p13 polarity, whose latency is in the range of 10 to 18 ms, and a subsequent n23 negative wave, which usually appears between 17 and 26 ms. The amplitude reflex shows an increase with an increasing intensity of tone bursts lasting up to 7–10 milliseconds which is followed by a decrease in amplitude. It is believed that this decrease in the amplitude response results from the activation of the stapedius reflex. Later response components (n34, p44) have a lower threshold of stimulation and are not of the vestibular (probably cochlear) origin. This short response latency (about 8 ms) indicates the transmission through oligosynaptic, possibly even via disynaptic ways, comprising primary vestibular afferent projections towards the complex of vestibular nuclei and over the medullary vestibular tract to the accessory nuclei [12–15].

The amplitude of p13–n23 varies considerably, from 25 μV to over 200 μV, so there are no reference values for this parameter. In this neurophysiological method, the amplitude is proportional to the contraction strength of the sternocleidomastoid muscle.

The reflex depends on the integrity of transmission of the middle ear, normal saccular anatomy, integrity of the lower vestibular nerve and central nervous system [16]. There are several ways to conduct VEMP measuring. There is the recommended intensity of an intensive click around 95–100 dB above the normal hearing threshold (the equivalent of 140 to 150 dB-SPL) well tolerated by patients. The existence of tinnitus is a relative contraindication for click and tone burst VEMP testing. In addition, the normal function of the conductive system is a prerequisite for performing VEMP. Specifically, it was found that the presence of even the smallest air-bone gap (7–8 dB) affects the attenuation of responses [17].

In this study, all healthy subjects had a response. The analysis of absolute latency of p13 waves defined their mean value of 15.18 ms (±1.24) and the mean value for n23 wave was 25 ms (±2.23). The analysis was made for the p13 latency of each side in men and women. It was concluded that the latency values of p13 right (15.26 ms ± 1.6) and left (15.10 ms ± 1.10) do not show any significant difference. There was no statistically significant difference in the correlation of latency values of p13 wave in men and women (right r = 0.012, p<0.05, left r = -0.142, p>0.05).

By analyzing the latency of n23 wave, it can be concluded that there is no significant difference between the right (24.75 ms ± 2.93) and left side (25.25 ms ± 1.98), nor there is any difference between the sexes (p > 0.05).

When using unilateral stimulation of SCM and electromyographic monitoring, the obtained latency values in the works of other authors are similar to those in this study. Wang et al. found the latency mean value of p13 to be 14.49 ms (± 1.28) and for n 23 it was 21.83 ms (± 1.65) [20]. Basta et al. describe the following values p13 16.2 ms (± 2.5) and n 23 wave of 24 ms (±2.6) [21]. Similar mean latency values of p13 and n23 waves were found in the study of Isaradisoikut et al. standing at 14.44 ms (±1.92) and 21.16 ms (±2.11), respectively [22]. In their research conducted by bilateral activation of SCM, Cheng et al. included 30 subjects, aged from 17 to 43, and presented the mean latency value of p13 wave to be 12.49 ms (± 0.94) and 19.79 ms (± 1.40) for the n23 wave [23].

Young et al. examined the right and the left side in their research and did not find any significant difference in the p13 wave latency (right 13.37 ms, left 13.53 ms). In addition, they did not notice any significant differences in the latency of n23 waves which was right ear 20.20 ms and left ear 20.58 ms [24].

The amplitude of the response is in proportion to the tonic electromyographic activity of m. ster-
nucleoideomastoideus and is less important for the clinical interpretation of responses [25].

In this study, the mean value of the amplitude was 88.85 μV (±38.37) right and 76.7 μV (±34.11) left, with no significant differences between the sexes.

The study of Carnauba et al., which included 40 subjects of both sexes, confirmed that there was no difference in latencies and amplitudes in either men or women. The latency of p13 for the right ear stood at 14.13 ms (±1.39) in women and 14.15 ms (±1.21) in men, and for the left ear, it was 14.14 ms (±1.42) in women and 14.35 ms (±1.41) in men. The n23 latencies were about 24 ms [26].

**Clinical Application of VEMP**

How important is VEMP test in the diagnosis of superior semicircular canal dehiscence (SCDS), impairment of the vestibular nerve, bilateral loss of vestibular function after ototoxic effects of aminoglycosides, central vestibular disorders, Meniere’s disease and hearing impairment?

VEMP is a useful method in patients with Tullio phenomenon, which is defined as vertigo provoked by a strong sound. It occurs in cases of superior semicircular canal dehiscence, perilymphatic fistula, Meniere’s disease, after surgery of fenestra and vestibulofibrosis. It is of particular importance in patients with fistula of the superior semicircular canal [27]. In this syndrome, VEMP responses register asymmetry in the amplitudes as well as the occurrence of very large amplitudes with the diagnosis of conductive hearing loss and the presence of air-bone gap. Having in mind that VEMP is sensitive to disturbed function of the saccule and reflex ways, Osch et al. applied this method in the diagnosis of vestibular neuritis, which occurred with the damage of lower vestibular nerve in their study [28].

In cases when the saccule is innervated by the lower branch of the vestibular nerve, the absence of VEMP response should be observed. However, during the VEMP test it is not possible to distinguish between the damage of the saccule and the vestibular nerve. If an inflammatory process covers the lower branch of the vestibular nerve, the lack of response is expected. When VEMP findings are changed in neuronitis of the vestibular nerve, the recovery and normalization of findings will happen faster than normalization of responses of lateral semicircular canal during caloric stimulation [29].

Therefore, VEMP can help to conclude how much of the vestibular nerve is affected, whether it is fully affected or the lower branch is spared. New clinical entity, neuritis of the lower branch of the vestibular nerve, can only be confirmed by VEMP. Sometimes, in rare cases, vestibular neuritis can affect only the lower branch of the vestibular nerve, and spare the upper one. Then the patient has no horizontal nystagmus, head-impulse test is negative, while the caloric test produces normal response. The only diagnostic tool which can explain the clinical picture of neuritis in these patients is VEMP. The absence of vestibulo-cervical reflex points to the fact that the lower branch of the vestibular nerve is affected by a pathological process. Murofuschi et al. found an abnormal VEMP finding in 25% of patients with neuronitis. It is believed that in this case, the first VEMP wave may simply be missing but the waves that occur later and are related to cochlear function have been preserved [30].

The complete absence of VEMP response is found in people with vestibular schwannoma, mutual loss of vestibular function after the use of aminoglycosides and after section of the vestibular nerve, when the importance of examining the residual function of the vestibular nerve after section of the same. In addition, no VEMP responses are observed in patients with otosclerosis [31].

After testing a large number of patients with the loss of vestibular function caused by aminoglycosides and without hearing impairment, Hain et al. included this test in the test battery of vestibular tests as a very good one [32]. Furthermore, there is no VEMP response in patients after instillation of gentamicin with unilateral Meniere’s disease [33].

Using VEMP with patients suffering from Meniere’s disease is of no importance since it reads the low amplitude on the side of the ear affected by disease [34]. The increase in response amplitudes in the early stage of Meniere’s disease, when there is a hearing fluctuation, is caused by dilatation of the saccule while the absence of responses indicates its collapse. The assumption that the VEMP response amplitude increases after Glycerol test or injections of furosemide indicates the existence of Meniere’s disease [35]. Controversial opinion of Hain et al. [32] states that the increase in the VEMP response amplitude is due to dilatation of the saccule and therefore, the opposite effect would be expected (decrease, not increase in response) after taking glycerol and furosemide.

The absence of vestibular evoked myogenic potential response and prolonged latency are encountered in patients with multiple sclerosis [36] and damage to the brain stem [37]. The most common pathological finding in these patients is prolonged P13 wave latency [38].

Function test of the lower part of the brainstem (medulla) is possible with vestibular evoked myogenic potentials while the early auditory evoked potentials of the brainstem are important for examination of function of the upper part of the same (pons and midbrain) [39, 40].

**Conclusion**

Vestibular evoked myogenic potentials is a relatively new diagnostic method that is applicable to patients with specific vestibular disorders and is a measurement of the inhibitory potentials during tonic contraction of the sternocleidomastoid muscle.
in response to intense sound stimulation. It is believed that the vestibular evoked myogenic potential response is of the vestibular origin. Vestibular evoked myogenic potential measuring is a simple, non-invasive method for examining the otolith organ function and functional integrity of the lower vestibular nerve. Normal function of the middle ear is a prerequisite for vestibular evoked myogenic potential measurement while a minimum reduction of conductive hearing compromises it. Vestibular evoked myogenic potential response is induced in people with sensorineural hearing loss.

Since vestibular evoked myogenic potentials is a new diagnostic method, it was necessary to make the standardization of response parameters. The mean value of the p13 wave latency in healthy subjects in this study was 15.18 ms (±1.24) and the mean value of n23 wave latency was 25.00 ms (±2.23). The amplitude mean value of the p13–n23 wave was 80.28 (±34.04) microvolts. No differences were observed in the values of latency and amplitudes between the right and the left ear. In addition, there were no differences in the values of the basic parameters of vestibular evoked myogenic potentials responses between men and women.

References

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