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Original Article

Can We Improve Pressure Feedback Methods in Vestibular Evoked Myogenic Potentials by Applying Custom Pressures?

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OBJECTIVE: The aim of the present study was to use constant and customized pressure levels to improve the feedback method of the blood pressure cuff technique in order to decrease intra-subject and inter-subject variability.

MATERIALS and METHODS: The study was conducted in two stages. In the first stage, the relationship between the pressure level generated in the blood pressure cuff and electromyographic response in the sternocleidomastoid (SCM) muscle was investigated. In the second stage, vestibular evoked myogenic potential (VEMP) measurements were made using a custom-built VEMP chair at a constant pressure level of 40 mmHg (P_{40}) or at 50% of the maximum pressure ($P_{max50\%}$) that could be generated by the SCM muscle.

RESULTS: VEMP measurements were performed on 100 volunteers consisting of 48 males and 52 females whose ages were between 20 and 68 years. The response rate was 41% on a subject basis and 53% on an ear basis. Response rates were similar in males and females, and they decreased with age. The response rate was significantly lower in 11% of the volunteers who could not generate the stipulated 80 mmHg pressure level. Response rates obtained with P_{40} and $P_{max50\%}$ were similar, and p13 and n23 latencies and p13-n23 amplitudes obtained from both sides were also similar. Amplitudes were higher in $P_{max50\%}$ measurements compared to P_{40}, and amplitudes obtained with P_{40} levels showed greater variance compared to $P_{max50\%}$.

CONCLUSION: The use of $P_{max50\%}$ provided reduced variation compared to P_{40}; however, it did not have significant clinical implications. Further studies are needed for the control of many factors that are related to amplitude variability.

KEYWORDS: Cervical vestibular evoked myogenic potential, vestibular function tests, saccule

INTRODUCTION

The use of vestibular evoked myogenic potentials (VEMP) as a vestibular test is relatively new, but due to its unique features such as providing information about the saccule and inferior vestibular nerves, it has gained a place in the standard vestibular test battery [1, 2].

Among the test parameters of VEMP, amplitudes are very important in the diagnosis of otologic diseases; however, high levels of inter-ear, inter-individual, and inter-laboratory variation complicates the clinical analysis of the results [3].

The VEMP amplitudes have been reported to vary depending on electromyographic (EMG) level of muscle strength, stimulus level, age, and sex [4, 5]. As a controllable and significant source of variation, the level of muscle contraction has been subjected to standardization efforts using feedback methods. The two main feedback techniques employed for this purpose depend on EMG response or muscle force. The measurement of muscle force using a blood pressure manometer was introduced as an effectual, cheap, and readily available method compared to the EMG techniques [6].

In the blood pressure manometer techniques, patients are asked to maintain a constant pressure when they squeeze the preinflated cuff in order to decrease inter-ear variation. However, a customized pressure level rather than a constant level might help to

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obtain better response rates and decrease inter-individual amplitude variation.

The aim of the present study was to investigate the efficacy of customized pressure levels on inter-ear and inter-individual amplitude variations by using a custom-made VEMP chair and blood pressure manometer method.

MATERIALS and METHODS

The study was conducted in Uludağ University School of Medicine in the departments of physiology and otorhinolaryngology between June 2011 and June 2013 with the permission of the Ethics Committee of the Uludağ University School of Medicine (2011-10/24).

Volunteers were invited into study from the employees and students of the institution and from relatives of patients in the otolaryngology clinic. Healthy volunteers who did not have any otologic, neurotologic, neurologic, or systemic diseases; complaints of hearing loss, balance, or any head and neck problems; or history of surgery or radiotherapy to the head and neck area were recruited into the study. Those who were found to have normal otolaryngological examination were informed about the study procedure, and written consent was obtained. Volunteers who were included in the second stage of the study were also investigated for normal (<25 dB HL) and symmetrical (≤10 dB HL) hearing thresholds in the pure tone audiometry involving 125, 250, 500, 1000, 2000, 4000, and 8000 Hz frequencies in air conduction and 500, 1000, 2000, and 4000 Hz frequencies in bone conduction. Audiological tests were performed with an Interacoustics AC-40 audiometer (Interacoustics AC, Assens, Denmark) in a silent cabin. Volunteers older than 65 years old who had hearing loss consistent with presbyacusis were included in the study provided that the hearing loss was bilaterally symmetric and not of sudden onset.

The study was planned in two stages. In the first stage, the relationship between the EMG voltages and the pressure level produced in the cuff of the blood pressure manometer was studied in order to identify the most appropriate pressure levels. In the second stage, VEMP tests were conducted at different pressure levels.

The first stage of the study was conducted on 32 volunteers, and the measurements were performed on an MP-30 system (Biopac Systems Inc., Goleta, CA, USA). Similar to electrode placement in the VEMP, the active electrode was placed on the 1/2 mid-portion of the sternocleidomastoid (SCM) muscle belly, the ground electrode was placed on the forehead, and the reference electrode was placed on the manubrium sterni. Ag/AgCl surface electrodes (Blue sensor, Ambu, Denmark) were attached to the skin after cleansing and scrubbing the skin with a dermabrasive gel (Nuprep, Weaver and Company, Aurora, CO, USA). The blood pressure cuff was held by the volunteer next to the chin without forcing. Volunteers were seated in an upright sitting position with their back resting on the back support of the chair. The head of the patient was flexed 30 degrees forward and rotated 30 degrees opposite to the tested SCM muscle without tilting the head. The volunteer was asked to squeeze the cuff, which was inflated to 20 mmHg, with their chin and cheek against their hand and to maintain the required pressure with the help of visual feedback from the pressure gauge. The device simultaneously recorded EMG and the pressure applied to the cuff (Figure 1). Before the measurement, the volunteer was asked to generate the maximum pressure that was possible to be maintained for at least 10 seconds. The EMG tracks were recorded for both sides at the maximum pressure level and at 75%, 50%, and 25% of the volunteer's maximum pressure level and at 40 mmHg constant pressure. A record of at least 10 seconds at a steady pressure was obtained. Root mean square (RMS) EMG voltages were calculated by the device. The relationship between pressure and RMS EMG was analyzed in different pressure levels.

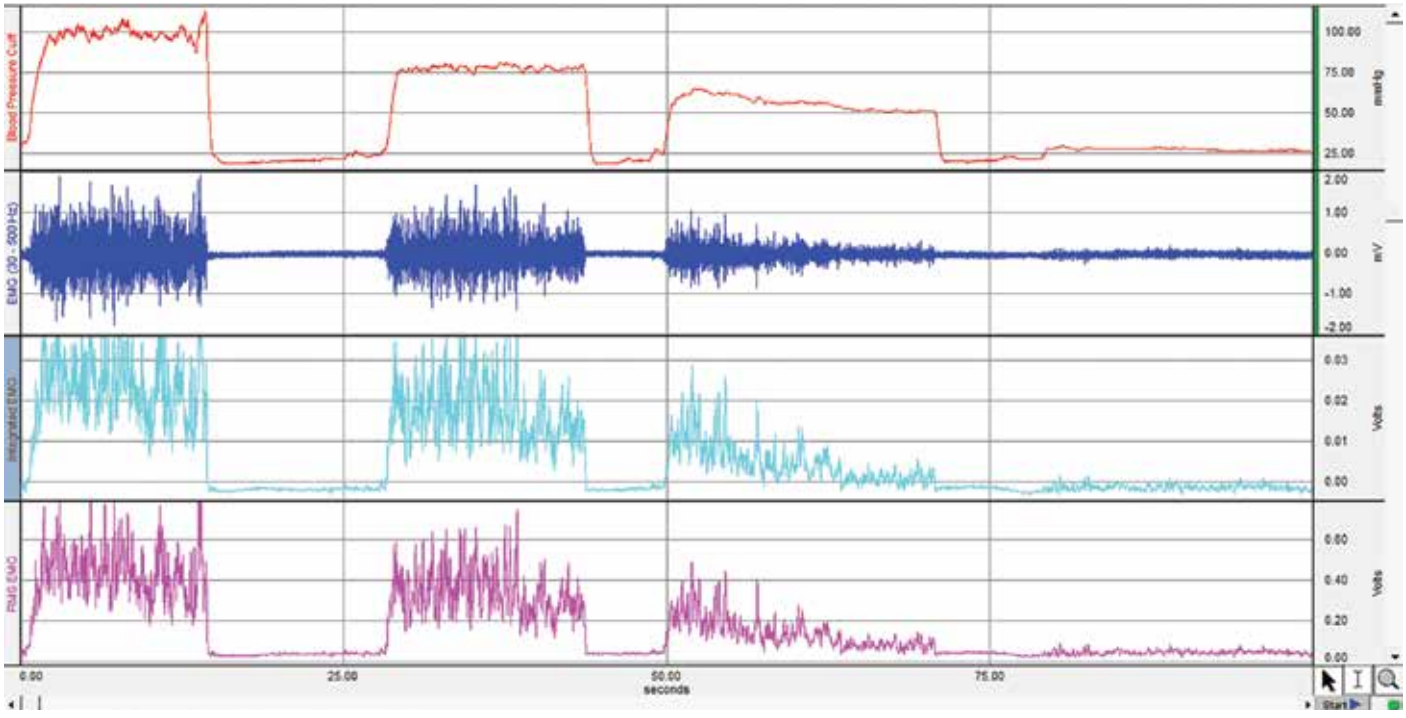

Figure 1. The results screen of the Biopac Student Lab PRO program. The upper part shows the generated pressure in the cuff, followed by EMG traces and the root mean square (RMS) EMG in the bottom part.

In the second stage, volunteers were selected to form three age groups of 20–29 years, 30–39 years, and >40 years each consisting of at least 10 persons. VEMP recordings were made in the second stage. A custom-made "VEMP Chair" was manufactured. It was designed to position volunteers in the desired position and to hold the cuff without using the hands. A standard clinical blood pressure manometer cuff (Erka Perfect-Aneroid, Bad Tölz, Germany) was attached to the arm of the VEMP chair (Figure 2a). The volunteer was seated on the chair, and the forehead, manubrium, and 1/2 mid-portion of both SCM muscle bellies were prepared with dermabrasive gel (Nuprep) in order to lower the impedances. A ground electrode was placed on the midline forehead, an active (inverting) electrode was placed on the manubrium, and reference (non-inverting) electrodes were placed on both SCM muscles. Gold electrodes were attached to the skin by EEG paste (Ten20, Weaver and Company) and taped into place. Insert-type earphones ER-3A (Etymotic Research Inc., IL, USA) were placed into the ear canals.

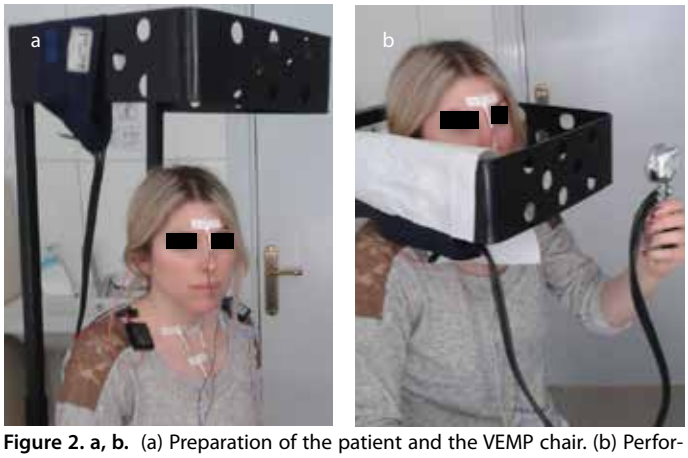

Figure 2. a, b. (a) Preparation of the patient and the VEMP chair. (b) Performance of the VEMP test.

The head of the patient was flexed 30 degrees forward and rotated 30 degrees opposite to the tested SCM muscle without tilting the head. The arm of the VEMP chair was adjusted to the height of the volunteer so as to hold the cuff next to the volunteer's chin and cheek (Figure 2b). The volunteer was asked to squeeze the cuff, which was inflated to 20 mmHg, with their chin and cheek against the cuff and to maintain the required pressure during the recording with the help of visual feedback from the pressure gauge. The operator also monitored the pressure level and warned the volunteer or aborted the test if necessary.

The VEMP tests were performed with an ICS Chartr EP-200 device (GN Otometrics, Schaumburg, IL, USA). Responses were acquired separately from each side using 90 dB nHL (120 dB SPL) 500 Hz short tone-burst (STB 500) stimuli (Blackman envelope: rise/fall time=2 cycles, plato=0 cycles). Responses to 150 stimuli given at a rate of 5 Hz were averaged. VEMP responses were amplified 5,000 times and band-pass filtered (10 Hz–1500 Hz). The analysis sweep time was 100 msec.

Before the test, the volunteers were asked to produce the maximum pressure they could generate on the blood pressure manometer. Measurements were performed at 40 mmHg constant pressure (P_{40}) and at 50% of the maximum pressure that was generated ($P_{max50\%}$). Peak-to-peak amplitude (p13-n23) and absolute latencies (p13 and n23) were analyzed for each measurement. The asymmetry ratio of the amplitudes of the right and left sides was calculated by the percent ratio of the difference of peak-to-peak amplitudes to the sum of peak-to-peak amplitudes. Additionally, the VEMP threshold was obtained at P_{40} by 10 dB decrements and 5 dB increments.

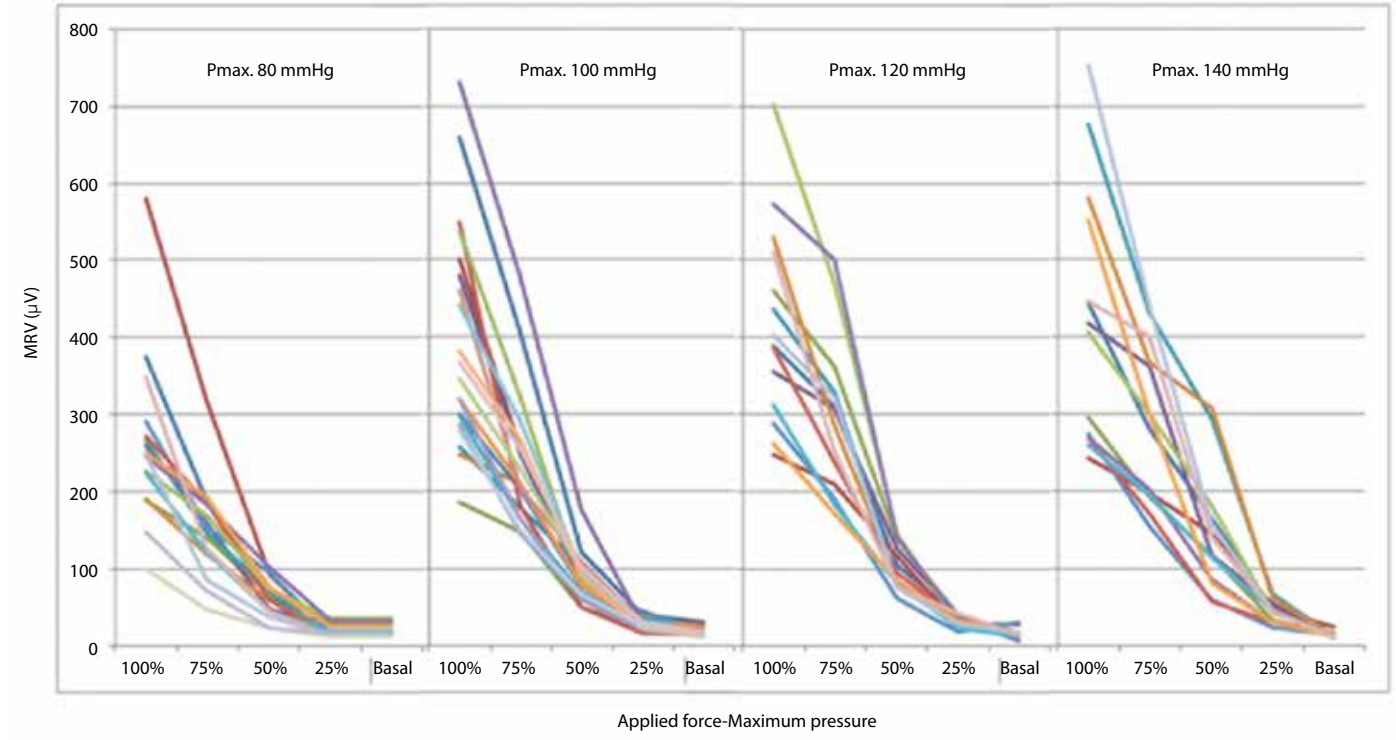

Figure 3. Maximum pressure levels and root mean square (RMS) EMG voltages obtained at 100%, 75%, 50%, and 25% of the maximum pressure and basal activity.

Table 1. Response rates and pressures generated by the subjects according to age and gender

				Response				
		Age	Maximum Pressure	Bi P	R P	L P	Bi N	Total
Age group	20-29	24.3±3.1	97.3±21.5	15	4	5	6	30
	30-39	34.6±2.6	100.5±21.3	14	3	2	11	30
	>40	50.2±7.9	90.3±20.8	12	1	8	19	40
Gender	Men	38.5±11.2	106.5±18.6	20	2	12	14	48
	Women	37.1±13.2	85.3±18.7	21	6	3	22	52
Total	37.7±12.3	95.5±21.4	41	8	15	36	100	

Bi P: bilateral positive; R P: right side positive; L P: Left side positive; Bi N: bilateral negative

Statistical Analysis

Statistical analysis of the data was performed using (Statistical Package for the Social Sciences for Windows, version 21 IBM Corp., Armonk, NY, USA). In the comparison of two independent groups, Student's t-test was used in case of continuous variables showing normal distribution, and the Mann–Whitney U-test was used if the distribution was not normal. Pearson's chi square was used for comparison of categorical variables. For comparison of more than two groups, the Kruskall–Wallis test was used. Dependent variables were compared with the Wilcoxon test. Correlation analysis was made using Spearman's rho, and variances were analyzed using the coefficient of variance. The level of significance was set to $p<0.05$.

RESULTS

1st Stage

The volunteers consisted of 8 women and 24 men between the ages of 21 and 43 years with an average age of 32 years. The maximum pressure produced in the blood pressure manometer was 80 mmHg in 8 volunteers, 100 mmHg in 10 volunteers, 120 mmHg in 7 volunteers, and 140 mmHg in 7 volunteers.

Root mean square EMG values were obtained at 100%, 75%, 50%, and 25% of the maximum pressure values (given that 25% of the maximum pressure was greater than 20 mmHg). The RMS EMG equivalent at a constant pressure of 40 mmHg pressure, which was used in previous studies, was also measured [6]. There was a direct relationship between the percent pressure levels and the RMS EMG values. However, as the muscle force increased, the value of RMS EMG was observed to increase exponentially (Figure 3). According to the hypothesis of the study, RMS EMG levels at $P_{max50\%}$ and P_{40} pressure levels were analyzed. The mean RMS EMG value was 96±50.9 mV at $P_{max50\%}$ and 56±17.9 mV at P_{40}. We found a strong correlation between the two sides of the same volunteer at $P_{max50\%}$ (r=0,797, p<0.001) and an average correlation at P_{40} (r=0.490, p=0.004). According to these results, we decided to use $P_{max50\%}$ and P_{40} pressure levels in the second stage of the study.

2nd Stage

The VEMP tests were performed in 100 volunteers consisting of 48 men and 52 women. The ages of the volunteers were between 20 and 68 years with a mean age of 38±12 years. Volunteers were grouped according to sex and the age groups of 20–29 years, 30–39 years, and 40 years and older (Table 1). The pressure levels produced by the SCM muscle were similar between the age groups (p=0.252), whereas women produced lower pressures than men (p<0.001).

In volunteers who produced 80 mmHg as the maximum pressure, $P_{max50\%}$ was equal to P_{40}. In 11 volunteers, the maximum pressure was even lower than 80 mmHg (50 mmHg in 3 volunteers, 60 mmHg in 6 volunteers, and 70 mmHg in 2 volunteers), all of whom were women. There was a significant difference between the mean ages of volunteers who produced at least 80 mmHg (36.7±11.4 years of age) and those who could not (45.9±16 years of age) (p=0.018).

Bilateral VEMP responses were acquired in 41 volunteers, 23 volunteers had unilateral responses, and 36 volunteers had no responses (Table 1). The response rate was found to be 53% on ear basis. The response rate was similar for sex (p=0.255) but was significantly lower in older volunteers (p=0.003). The mean age was 33.3±8.6 years in those who had bilateral responses, 38±14 years in those with unilateral responses, and 42.6±13 years in those who did not have any responses. Maximum pressure level was not found to be effective on response rate (p=0.374). The mean maximum pressures were 97.8±18.1 mmHg in subjects with bilateral responses, 95.2±13.1 mmHg in subjects with unilateral responses, and 92.9±28.3 mmHg in subjects with no responses. However, there was a difference in the response rate between those who could (52.8%) and could not (18.2%) generate the maximum pressure level of 80 mmHg (p=0.002). The response rate was not different between the measurements performed at P_{40} (50.8%) and $P_{max50\%}$ (53.8%) (p=0.622).

At $P_{max50\%}$, the p13 latencies were 16.5±1.9 msec for the right side and 16.4±1.8 msec for the left side. At P_{40}, the right and left p13 latencies were 16.6±1.8 msec and 16.7±2 msec, respectively. The right and left side n23 latencies were 24.5±1.7 msec and 24.2±1.5 msec at $P_{max50\%}$ and 24.6±1.8 msec and 24.5±1.4 msec at P_{40}, respectively. Latencies were similar for both sides when analyzed as independent variables (all left sides vs. all right sides) and dependent variables (right and left sides of the same individual). There were no differences in latencies between VEMPs acquired in P_{40} and $P_{max50\%}$ measurements.

The p13-n23 amplitudes for the right and left sides were 94.2±57.5 μV and 101.5±58.4 μV at $P_{max50\%}$ and 68±45.8 μV and 66.5±48.9 μV at P_{40}, respectively. There were no differences in p13-n23 amplitudes between the right and left sides for either $P_{max50\%}$ or P_{40} measurements when analyzed as independent variables (all left sides vs. all right sides) (p=0.577 and p=0.757) or as dependent variables (right and left sides of the same individual) (p=0.694 and p=0.388), respectively.

Amplitudes were higher in $P_{max50\%}$ measurements compared to P_{40} measurements (p<0.001). Amplitudes at $P_{max50\%}$ demonstrated an upward trend until 100 mmHg maximum pressure and then remained

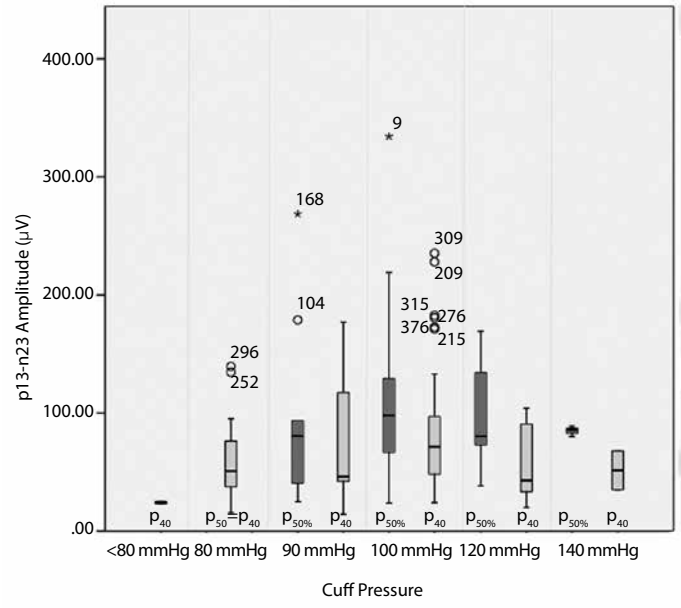

Figure 4. Changes in p13-n23 amplitudes obtained with $P_{max50\%}$ and P_{40} measurements according to the maximum pressure produced.

Table 2. p13-n23 amplitudes according to age groups, sex, and maximum pressure generated

		p13-n23 Amplitudes (µV)	
		p_{40}	$p_{max50\%}$
Age group	20-29	69.7±41.4	103.7±63.7
	30-39	46.9±23.9	83.6±45.2
	40-69	84.5±62.3	117.2±72.1
		p=0.015	p=0.303
Gender	Men	64.8±44.5	97.8±46.7
	Women	70±50.6	108±79.9
		p=0.472	p=0.797
Total		67.2±47.2	102.1±62.4

constant in the upper pressures. In contrast, amplitudes obtained at P_{40} showed roughly a constant level throughout the pressure spectrum but with more variability (Figure 4). The amplitudes obtained in volunteers who produced different maximum pressure levels were similar for $P_{max50\%}$ (p=0.333), but this was not true for P_{40} (p=0.013). The coefficient of variance for the p13-n23 amplitude was higher in P_{40} measurements (67.5%) compared to $P_{max50\%}$ measurements (51%).

There were no differences in p13-n23 amplitudes according to sex. For age groups, amplitudes were similar at $P_{max50\%}$ but were lower in the 30–39 year age group at P_{40} (p=0.015) (Table 2).

Asymmetry ratios were calculated as 0.238±0.161 in P_{40} and 0.279±0.142 in $P_{max50\%}$ measurements, and these were not significantly different (p=0.935). Asymmetry ratios were not different for age or sex.

Stimulus thresholds were similar for right ears (83.90±6.18 dB HL) and left ears (83.41±6.84 dB HL) and did not differ according to age or sex. Stimulus thresholds of 18 volunteers were the same in both ears. There was a 5 dB interaural difference in 12 volunteers, a 10 dB difference in 7 volunteers, and a 15 dB difference in 4 volunteers.

DISCUSSION

Vestibular evoked myogenic potentials provide information regarding the saccule and inferior vestibular nerves, which makes it an important part of the vestibular test battery. However, VEMP is an inhibitory response, and good muscle contraction is a prerequisite for its recording. The level of muscle contraction causes great variations in the results, and with the addition of other variables VEMP parameters become difficult to analyze.

The first part of the present study demonstrated that the relationship between muscle tension and EMG activity was a complex one. Due to its exponential nature, it is not easy to predict a suitable level of muscle tension just by looking at pressure levels; however, we decided that 50% of maximum pressure was a suitable level for our purpose.

In order to obtain a steady muscle tension, the test may be performed when the patient raises and rotates their head when lying in a recumbent or semi-recumbent position. This position was proposed to be ideal because it provided the largest VEMP amplitude and highest rate of test-retest reliability [7-9]. However, the compliance might be lower, especially in older patients [9]. Testing in a sitting position was reported to be more comfortable and tolerable. Multiple repeats of the test became necessary to obtain all parameters, which made a sitting position more advantageous. However, sustained, sufficient muscle activation needs additional precautions, especially in a sitting position [9]. Additionally, a reliable comparison of the results of the right and left sides requires control of EMG activity during the test.

Two methods were developed for controlling and adjusting the level of EMG activity on the VEMP results. One of these methods was auditory or visual feedback to control the muscle tension [1]. The other method was mathematical correction of evoked potential amplitudes according to EMG activity (normalization) [10]. Both techniques provided some benefit, but the results were still not optimal [11-15].

Other problems with specific EMG systems are cost and unavailability of these devices. Vanspauwen et al. [6] offered a solution for this problem by using a blood pressure manometer, which is readily available in every clinic, for visual feedback of muscle tension.

Vanspauwen et al. [6] asked the patients to squeeze the cuff of the blood pressure manometer, which they were holding in their hands, to a constant 40 mmHg pressure with their chin and cheek. Maes et al. [16] further improved this technique by fixing the cuff to a stable bar, thereby preventing the interference of the hand holding the cuff. Inspired from these studies, we designed a custom-made VEMP Chair in order to optimally position the patient and the blood pressure cuff. The VEMP Chair was found to be practical in the performance of the VEMP test in a sitting position.

The p13-n23 amplitudes are the most important variables of the VEMP test for the diagnosis of vestibular disorders. However, these amplitudes are subject to large inter-subject and intra-subject (inter-ear) variation. Besides the saccular function, which is the purpose of the test, the stimulus level, muscle contraction, muscle mass, age,

electrode position, and test position have all been reported as factors affecting amplitudes [10, 13, 17, 18]. Moreover, Chang et al. [19] reported VEMP amplitudes to be inversely related to the subcutaneous tissue thickness in adults.

In routine practice, the VEMP test is analyzed by comparing results obtained from the right and left sides of the subjects. Intersubject comparison is a relatively indeterminate issue, and van Tilburg et al. [20] demonstrated that normalization significantly reduced the intersubject coefficient of variation by 50%. The primary aim of the present study was to decrease the intersubject variations by using customized muscle tensions. Compared to P_{40}, $P_{max50\%}$ provided lower coefficients of variation; however, the variance was still high for $P_{max50\%}$, probably due to many other factors governing the relationship between the generated muscle tension and the recorded electrical activity. Moreover, the advantage provided by $P_{max50\%}$ would offer little, if any, benefit in clinical practice because none of the different pressure levels were superior to others either in the right and left side comparisons of amplitudes or in response rates.

The VEMP results were found to be similar in men and women, which was consistent with the literature. Age, on the other hand, was reported to affect the VEMP results, and amplitudes are expected to decrease with age [21]. VEMP waves were reported to diminish and even to disappear after 60 years of age, and latencies increase with age [7, 10, 22-25]. In accordance with the literature, the response rate was found to decline as age increased in the present study. Age might affect VEMP due to changes in the vestibular system or the SCM muscle. Otolith functions have been found to diminish by 40 years of age [24, 26], and these findings are supported by morphological studies showing hair cell loss [27], vestibular nerve fiber loss [28], and neuron loss in Scarpa's ganglion [29]. Loss of muscle fibers, axons, and motor neurons has also been reported [30, 31]. The amplitudes were greater in the elderly subjects in the present study. However, we did not consider subjects without response when analyzing the amplitudes, and the ages of our subjects might not be that high. Nevertheless, we found a significant difference in p13-n23 amplitudes between age groups. The p13-n23 amplitudes were lower in the 30–39 year age group, which was significant only when the tests were performed at P_{40}. Interestingly, this group was also the one that generated the highest muscle tension. Because VEMP amplitudes depend on the tonic activity of the muscle [32], we suspect that lower levels of EMG activity were produced at constant pressure due to lower activity of the muscle.

Vestibular evoked myogenic potential response rates have been reported to be as high as 100%, but lower rates have been seen [33]. Insufficient muscle activity is a factor explaining the lack of response, and lack of sufficient muscle tension might be one of the reasons for this. Indeed, it has been shown previously that head rotation had a response rate of 70% in a study where head elevation had a response rate of 100% [9]. Muscle tension tended to be lower in individuals without response in our study. Eleven percent of the volunteers were not capable of producing the stipulated 80 mmHg pressure, all of whom were elderly women. On the other hand, there were subjects with no VEMP response even though they produced sufficient muscle activity. Simultaneous monitoring of EMG activity would provide insight into this dilemma, which was a shortcoming of the present study. Moreover, we suspect that the stimulus level might have been insufficient. STBs presented at the level of 90 dB HL (the maximum output level of the equipment) might be responsible for a lower response rate, and increasing the stimulus rate from 95 dB to 98 dB was reported to improve the response rate [33]. In another study, a VEMP response was acquired in all of 32 patients with 105 dB HL, whereas with a 90 dB HL stimulus a VEMP response was found only in 18 of them [34].

Stimulus thresholds were introduced as a new test parameter. Shin et al. [35] reported stimulus thresholds of 76±5 dB (65 dB–90 dB) and a highest interaural threshold difference of 10 dB for a 500 Hz STB stimuli. In the present study, the stimulus threshold was 83±6 dB and the highest interaural threshold difference was 15 dB.

In conclusion, the use of $P_{max50\%}$ provided reduced variation compared to P_{40}, but it did not prove to have significant clinical implications. Further studies are needed for the control of many factors that are related to amplitude variability.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Uludağ University Medical School.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ö.A.Ö.; Design - Ö.A.Ö., K.Ö., S.Ö., O.B.; Supervision - K.Ö., O.B.; Resources - Ö.A.Ö.; Materials - Ö.A.Ö.; Data Collection and/or Processing - Ö.A.Ö.; Analysis and/or Interpretation - Ö.A.Ö.; Literature Search - Ö.A.Ö., S.Ö.; Writing Manuscript - Ö.A.Ö.; Critical Review - K.Ö., S.Ö., O.B.

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