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Research Article

Evaluation of Hearing Loss in Behcet's Disease By High Frequency Audiometry, Auditory Steady-State Response (ASSR), Auditory Brainstem Response (ABR), and Vestibular Evoked Myogenic Potentials (VEMP)

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Introduction

Behcet's disease (BD) was first defined by the Turkish dermatologist Prof. Dr. Hulusi Behcet in 1937 and is a vasculitic disease that manifests itself with the classical triad of eye inflammation and oral and genital ulcers. In BD, along with mucocutenous involvement, involvement of other systems such as joints, vascular system, gastrointestinal system, and central nerve system can be observed, too. Although there are no pathognomonic laboratory findings, the disease can be diagnosed based on the clinical criteria. Risk of blindness due to ocular involvement is the most important reason for morbidity.

In 1924, Hulusi Behcet encountered a patient with recurrent aphthous stomatitis, genital ulcer, erythema nodosum, and visual impairment. After the first patient, he encountered a second in 1930 and a third in 1936, which led him to claim that the findings for these three patients were all associated with a specific disease. In 1937, he wrote his ideas in the *Archives of Dermatology and Syphilology* and *Dermatologische Wochenschrift* and that same year, he presented his findings at the meeting of the Dermatology Association of Paris. In 1947, at the suggestion of Prof. Mischner of the Zurich Medical Faculty during the International Medical Congress of Geneva, the findings of Behçet were named "Morbus Behçet." Later the naming was changed to Behçet's Syndrome and Trisymptom Behçet. Today, the disease is usually called Behcet's Disease [1-3].

Auditory Steady State Responses (ASSR) are the evoked potentials obtained by steady stimuli instead of transient ones. While measuring ASSR, a stimulus is presented periodically and monitored to see how the brain follows these stimuli or how the stimulus drives a response. These responses represent the synchronous discharge of auditory neurons in the brainstem, depending on the phase of the modulation frequency of the stimulus and they are the steady effects of the repeated stimuli [4,5].

The technique for measuring the responses is based on the statistical evaluation of the wave amplitude or the electrophysiological behavior generated by the frequency-modulated pure tone. Statistical techniques help differentiate the responses from the background noise and then recognizing the response. Studies undertaken suggest modulation frequencies of 75–100 Hz in children and adults [6,7]. When a lower rate is used in awake adults, increasing the wave amplitudes is perceived as an additional option as this facilitates an easier detection of the responses [8].

When a high modulation frequency is used, the characteristic of ASSR shows a resemblance to the auditory brainstem responses (ABR), which is another objective method used in the evaluation of hearing. ABR is a reliable method that is difficult to use with babies, but has been used for years with adults and children. However, the various limitations of the method do not enable obtaining frequency-specific data at all times, and the techniques used to obtain frequency-specific data prolong the duration of the test.

ASSR is superior to ABR in the following aspects:

(1) ASSR is a simple measurement tool. The wave amplitude and phase of the response to the stimulus frequency are recorded automatically by the computer. As it is no need to evaluate the waves in the responses, there is no need for an interpreter.

(2) The processes used to understand whether there is a response or not leave no room for interpretation. The techniques compare the response at modulation frequency and the noise generated at close frequencies and check the reliability of the response.

(3) ASSR yields frequency-specific information. The frequency of the amplitude modulation is concentrated on the pure tone frequency. The two side-bands of the tone are separated from the frequency through the frequency of the modulation signal.

When transient stimuli are used, as in ABR, there is a greater energy distribution from the short-term pure tone frequency to the other frequencies. Masking makes the process more complicated and prolongs the duration of the test[4,5,9,10].

ASSR measurement is a technique that has been studied intensely during the past 10 years. Although these studies give clues on using ASSR in frequency-specific determination of the level of hearing loss, there is still no international standard and therefore the studies on the reliability of this method are still in progress. In audiology, auditory evoked potentials are defined as the activity of the hearing system in response to an auditory stimuli. The vestibular evoked myogenic potentials (VEMP) technique is one of the electrophysiological measurement methods that has been used widely in recent years. VEMP, claims to originate in the saccule, and is a short latency electromyogram recording of the responses obtained by surface electrodes placed over the tonically contracted sternocleidomastoid (SCM) muscle [11].

Developing a method to obtain reliable VEMP recordings and normative data and comparing these data would help when using VEMP in clinical settings [12]. Each clinic has to ensure test standardization and establish normative data. Conducting standardization studies undertaken at different clinics would maximize the clinical use and create a common basis to evaluate VEMP findings in differential diagnoses.

The aim of the present study is to compare the estimated hearing threshold levels obtained by ASSR and the threshold levels obtained by ABR and pure tone threshold audiogram and to test the reliability with patients having Behcet's disease. This would stablish normative data by creating the best practices and recording parameters for Vestibular Evoked Myogenic Potentials and put VEMP test into practice as a differential diagnosis test in clinical settings.

Materials And Methods

In order to conduct the present study, an approval was obtained from the Research Ethical Committee of Cumhuriyet University's Faculty of Medicine. Eleven patients (six males, five females) clinically diagnosed with Behcet's disease were included to the study. All the patients were Turkish.

Eleven healthy individuals (six females, five males) having no complaints were randomly assigned to the control group.

No intervention violating the personal physical integrity of the participants was employed in the present study.

Before the Auditory Steady-State Response (ASSR) and Vestibular Evoked Myogenic potentials (VEMP) tests, the patients underwent pure tone audimotery (PTA) and auditory brainstem response (ABR) tests.

An AC 40 Interacoustic Clinical Audiometer™ and TDH-39P Telephonic HB-7 earphones™ were used for the PTA test, while the high-frequency audiometry analysis was performed using an AC 40 Interacoustic Clinical Audiometer™ and Koss digital earphones R/80™.

The practices of the American National Standards Institute (ANSI) were observed in terms of the hearing level, and a hearing level above 26 dB was regarded as a pathology.

The Otometrics ICS chart EP 200 was used for the VEMP, ASSR, and ABR tests.

The test stimuli were placed into the participants' ears by the aid of a soft probe, and electrodes used for recordings were placed on their forehead, vertex, and the earlobe of the test

ear. A click stimulus (stimulation level: 40 db nHL) was used in ABR test.

The test duration of ASSR took approximately 20 minutes in one ear. The patients were asked to lie down comfortably on the test coach and move as little as possible during the test.

Tests were initiated using the pure tone hearing threshold levels obtained at each frequency. When no response was obtained, the starting intensity of the test tone was increased in 10db steps. After a response was obtained, the threshold level was detected by decreasing the intensity of the test tone in 5db steps. The lowest level of the two responses was taken as the threshold.

For VEMP responses, the latency and amplitude values of P13 and N23 waves and mean VEMP threshold were detected. The participants laid down in a supine position in a quiet room and were instructed to rotate their heads to the side contralateral to the stimulated ear when the stimulus was presented, which would contract the SCM muscle of the stimulated ear. Stimuli were presented monaurally to the right and left ears and the electromyogenic (EMG) activity of the SCM muscle was recorded ipsilaterally. During the test, the electrode impedance was not allowed to go below 5,000 ohm.

In VEMP, the earth electrode was placed on the forehead, the active electrode was placed over the middle of the sternocleidomastoid muscle, and the reference electrode was placed over the sternum at the sternocleidomastoid muscle. Responses given to the stimuli at 500 Hz and 1,000 Hz tones were compared. When a 500-Hz burst was used, the morphology of the P13-N23 wave was observed to be more significant and thus, for the study, we decided to continue using a 500-Hz tone burst stimulus.

(Figure 1). All the individuals were subjected to a stimulus presented at an intensity level of 90 dB nHL.

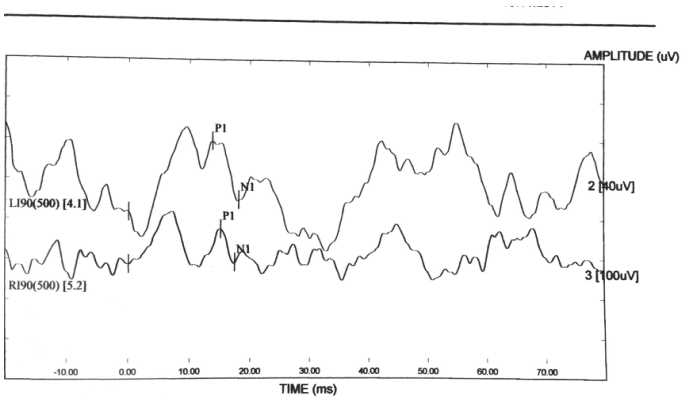

Figure 1. Sample VEMP responses obtained by using 500 Hz tone burst stimulus.

Results

The average age was 39.81±11.61 years in the patient group and 37.63±13.37 years in the control group. The groups did not have a significant difference in terms of age (P=0.687; P>0.05).

Of the individuals in the patient group, six (54.5%) were males and five (45.5%) were females. In the control group, there were five (45.5%) males and six (54.5%) females. In terms of gender, the groups did not show any significant difference (P= 0.67 : P> 0.05).

In the patient groups, the mean number of days to recurrence was 16.27±24.40 days, the mean duration of disease was 14.63±10.63 years, and the mean ulcer diameter was 7.81±2.27 mm. In the patient group, one (9.1%) patient had diabetes mellitus, two (18.3%) patients had hypertension, while eight had no concomitant disease.

In the VEMP test, there was no difference between the groups when P13 and N23 wave latencies and PN amplitudes were compared (Table 1).

Table1. Intergroup comparison of VEMP test data between the groups.

	grups	Mean	Std. Deviation	p
right p13 lat	patient	20,00	5,56	0,788
	control	19,28	6,61	
right n23 lat	patient	25,5755	6,41186	0,826
	control	26,2873	8,42215	
right pn amp	patient	63,5964	56,93663	0,072
	control	118,8682	77,90085	
left p13 lat	patient	21,5455	4,03857	0,159
	control	18,3636	5,96705	
left n23 lat	patient	26,5000	6,41875	0,631
	control	25,1982	6,09402	
left pn amp	patient	82,0127	88,07687	0,738
	control	93,1420	56,77764	

Lat: latencie

Amp: amplitude

When the pure tone audiometry (PTA) data of the groups were studied, the right ear data were significantly different at 500 Hz, 6,000 Hz, 8,000 Hz, 12,000 Hz, and 16,000 Hz, while those at 1,000 Hz, 2,000 Hz, and 4,000 Hz did not show any significant difference (Table 2).

Table 2. Intergroup comparison of right ear PTA data.

	grups	Mean(dBHL)	Std. Deviation	p
right PTO 500 hz	patient	17,2727	7,19848	0,040*
	control	11,8182	4,04520	
right PTO 1000 hz	patient	15,4545	9,60587	0,082
	control	10,0000	2,23607	
right PTO 2000 hz	patient	14,5455	10,35725	0,170
	control	10,0000	2,23607	
right PTO 4000 hz	patient	16,8182	13,09059	0,102
	control	9,5455	5,22233	
right PTO 6000 hz	patient	25,4545	17,38599	0,047*
	control	13,6364	6,36039	
right PTO 8000 hz	patient	34,0909	26,62876	0,044*
	control	15,9091	8,89331	
right PTO 12000 hz	patient	41,3636	20,38270	0,001*
	control	12,2727	8,17424	
right PTO 16000 hz	patient	48,6364	13,24593	0,001*
	control	15,9091	9,70005	

PTA: pure tone audiometer

When the pure tone audiometry (PTA) data of the groups were studied, the left ear data were insignificant at 500 Hz, 2,000 Hz, and 16,000 Hz, while those at 1,000 Hz, 4,000 Hz, 6,000 Hz, 8,000 Hz, and 12,000 Hz showed a significant difference (Table 3).

Table 3. Intergroup comparion of left ear PTA data.

	groups	Mean(dBHL)	Std. Deviation	p
left PTA 500 hz	patient	19,0909	8,89331	0,053
	control	12,7273	4,67099	
left PTA 1000 hz	patient	17,2727	9,83962	0,027*
	control	10,0000	2,23607	
left PTA 2000 hz	patient	16,8182	10,55290	0,060
	control	10,0000	2,23607	
left PTA 4000 hz	patient	19,0909	11,79368	0,023*
	control	9,5455	5,22233	
left PTA 6000 hz	patient	27,7273	15,71045	0,023*
	control	14,5455	6,50175	
left PTA 8000 hz	patient	32,7273	26,11165	0,046*
	control	14,0909	9,95444	
left PTA 12000 hz	patient	39,0909	18,94969	0,001*
	control	14,0909	7,35465	
left PTA 16000 hz	patient	51,3636	10,50974	0,001*
	control	18,1818	14,53835	

PTA: pure tone audiometer

When the ASSR data were studied, the parameters differed significantly at all frequencies (500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz) in the right ear, while the left ear parameters showed a significant difference at 500 Hz and 400 Hz and a non-significant difference at 1,000 Hz and 2,000 Hz (Table 4).

Table 4. Intergroup comparison of ASSR data.

	grups	Mean(dBHL)	Std. Deviation	p
right ASSR 500 hz	patient	41,8182	4,04520	0,023*
	control	33,6364	10,26911	
right ASSR 1000 hz	patient	33,6364	11,20065	0,019*
	control	20,9091	12,21028	
right ASSR 2000 hz	patient	38,1818	14,70930	0,015*
	control	21,8182	14,01298	
right ASSR 4000 hz	patient	45,4545	11,28152	0,002*
	control	28,6364	10,97518	

left ASSR 500 hz	patient	40,0000	10,00000	0,018*
	control	29,5455	9,07043	
left ASSR 1000 hz	patient	40,0000	18,97367	0,228
	control	31,3636	13,05582	
left ASSR 2000 hz	patient	31,8182	12,50454	0,254
	control	25,4545	12,93340	
left ASSR 4000 hz	patient	43,6364	16,29278	0,014*
	control	27,2727	11,90874	

ASSR: auditory steady state responses

When the ABR data were studied, the parameters of both ears showed a non-significant difference (Tables 5 and 6).

Table 5. Intergroup comparison of right ear ABR data.

	grups	Mean	Std. Deviation	p
right 1.amp (µv)	patient	,0991	,08276	0,212
	control	,0655	,02505	
right 1.lat (ms)	patient	1,9064	,51833	0,054
	control	1,5100	,38042	
right 3.amp (µv)	patient	,0827	,05331	0,093
	control	,1245	,05768	
right 3.lat(ms)	patient	4,8600	,62538	0,294
	control	4,5736	,62052	
right 5.amp(µv)	patient	,2145	,09103	0,063
	control	,3145	,14187	
right 5.lat(ms)	patient	6,6318	,60732	0,067
	control	6,1982	,42888	
right 13interpik(ms)	patient	2,9545	,62745	0,695
	control	3,0627	,64733	
right 15interpik(ms)	patient	4,7236	,65841	0,518
	control	4,5082	,86196	

amp: amplitude

Table 6. Intergroup comparison of left ear ABR data

	grups	Mean	Std. Deviation	p
left 1.wave amp.(µv)	patient	,0718	,02562	0,516
	control	,0818	,04309	
left 1. wave lat. (ms)	patient	1,7482	,35516	0,164
	control	1,5500	,28408	
left 3. wave amp. (µv)	patient	,1209	,05683	0,207
	control	,1518	,05419	
left 3. wave lat. (ms)	patient	4,6855	,48731	0,693
	control	4,5873	,64999	
left 5. wave amp(µv)	patient	,2464	,09760	0,103
	control	,3736	,22655	
left 5. wave lat(ms)	patient	6,8236	,58469	0,052
	patient	6,2909	,52260	
left 1-3 interpik lat(ms)	patient	2,9209	,47861	0,529
	control	3,0555	,50623	
left 1- 5interpik lat(ms)	patient	4,9118	,69110	0,287
	control	4,5309	,92422	

amp: amplitude

The intragroup comparison of the SSO and ASSR data of the individuals in both groups revealed significant differences in the right ear parameters (Table 7).

Table 7. Intragroup comparison of PTA and ASSR data

grups			Mean (dBHL)	Std. Deviation	p
patient	Pair 1	right pta 500hz	17,2727	7,19848	0,001*
		right assr 500hz	41,8182	4,04520	
	Pair 2	right pta 1000 hz	15,4545	9,60587	0,001*
		right assr 1000 hz	33,6364	11,20065	
	Pair 3	right pta 2000 hz	14,5455	10,35725	0,001*
		right assr 2000 hz	38,1818	14,70930	
	Pair 4	right pta 4000 hz	16,8182	13,09059	0,001*

		right assr 4000 hz	45,4545	11,28152	
control	Pair 1	right pta 500 hz	11,8182	4,04520	0,001*
		right assr 500 hz	33,6364	10,26911	
	Pair 2	right pta 1000 hz	10,0000	2,23607	0,011*
		right assr 1000 hz	20,9091	12,21028	
	Pair 3	right pta 2000 hz	10,0000	2,23607	0,016*
		right assr 2000 hz	21,8182	14,01298	
	Pair 4	right pta 4000 hz	9,5455	5,22233	0,001*
		right assr 4000 hz	28,6364	10,97518	

Assr: Auditory Steady-State Response

Pta: pure tone audiometer

Similarly, the intragroup comparison of the SSO and ASSR data of the individuals in both groups revealed significant differences in the left ear parameters (Table 8).

Table 8. Intragroup comparison of left ear PTA and ASSR data.

grups			Mean (dBHL)	Std. Deviation	p
patient	Pair 1	left pta 500 hz	19,0909	8,89331	0,001*
		left assr 500 hz	41,8182	4,04520	
	Pair 2	left pta 1000 hz	17,2727	9,83962	0,001*
		left assr 1000 hz	40,0000	18,97367	
	Pair 3	left pta 2000 hz	16,8182	10,55290	0,003*
		left assr 2000 hz	31,8182	12,50454	
	Pair 4	left pta 4000 hz	19,0909	11,79368	0,001*
		left assr 4000 hz	43,6364	16,29278	
control	Pair 1	left pta 500 hz	12,7273	4,67099	0,001*
		left assr 500 hz	33,6364	10,26911	
	Pair 2	left pta 1000 hz	10,0000	2,23607	0,001*
		left assr 1000 hz	31,3636	13,05582	
	Pair 3	left pta 2000 hz	10,0000	2,23607	0,002*
		left assr 2000 hz	25,4545	12,93340	
	Pair 4	left pta 4000 hz	9,5455	5,22233	0,001*
		left assr 4000 hz	27,2727	11,90874	

lat: latencie

The data obtained in our study were loaded on SPSS 14.0 software, and an unpaired t-test and paired t-tests were used when the parametric test assumptions were met, while a Man Whitney-U test, Wilcoxon test, and Chi-square test were used when the parametric test assumptions were not met. Significance level was taken as 0.05.

Discussion

The results obtained with ASSR and SSO at 500 Hz, 1000 Hz, 2,000 Hz, and 4000 Hz showed a statistically significant but low correlation between the subjects participating in the study. The ASSR test usually yields information on the hearing level; however, the values obtained are not the same with the ones obtained by pure tone audiogram. To illustrate, when the pure tone threshold is found to be 10 dbHL, then the ASSR thresholds are sometimes 25 dbHL, sometimes 15 dbHL, and sometimes 40dbHL. The same is true for the other frequencies. Although both of these tests yielded normal hearing values within their own criterion, variations between subjects affected the consistency between the thresholds. Okumusoglu Sayar reported results similar to the ones obtained in the present study [13].

On the other hand, in individuals having normal hearing, the ASSR and pure tone audiogram values are highly correlated [4,10,14,15,16]. Possible reasons of such a discrepancy can be [1] The parameters used can be different from the parameters reported in other studies as the subjects are awake [8]. Results obtained in studies given in the references were obtained from sleeping subjects and employed a higher modulation frequency. [2] Findings are similar to those of Luts and Wouters who conducted a similar study [17]. [3] Test environment could be affecting the awakening status of the subjects. In the present study, a soundproof room was setup not as an experimental area but as a clinic suitable for routine audiology practices. It is possible that the subjects were affected by the increasing noise outside of the clinic. Based on the findings obtained in our study, it can be reported that the ASSR test performed using the parameters in our study cannot be used in predicting the pure tone audiogram threshold levels in individuals with normal hearing.

To evaluate the reliability of ASSR in individuals having normal hearing, the same patients were studied using tone-burst ABR and ASSR [18]. It was reported that standard ABR and ASSR yielded consistent results of 2,000–4,000 Hz, but the standard Hz fell short in determining the threshold at low frequencies. It was reported that there was no statistical difference between the results obtained by ASSR test and tone-burst ABR at a frequency of 41 Hz MF [19]. It was also reported that ABR and ASSR may show a 20-db difference in the thresholds of individuals having a normal hearing [18,20].

ASSR shows the hearing loss within the limits of the hearing loss and it is possible to determine the degree of the hearing loss. However, the test fails in predicting the threshold obtained in pure tone audiogram and ABR, and wrong outcomes are generated when the thresholds are evaluated only by ASSR. The results obtained in the present study testing the reliability of ASSR, which is a newly developed technique and therefore

not yet common in practice, by comparing it to other tests with established standards and used for many years show that using ASSR as part of an audiology evaluation would yield some information about the hearing level, but when it is used alone in determining the threshold levels, it should be taken into account that there may be some differences with a high variation in threshold levels among the subjects when compared to the standard tests.

In the literature, there are many studies on VEMP practices. In these studies, electrode localization, applied parameters, and study findings differ.

In single-channel electrode placement, Petrak placed the active electrodes over the middle of the SCM muscle, reference electrodes over the sternoclavicular joint (near collarbone), and earth electrodes over the contralateral SCM muscle or forehead [21].

In our study, we found that electrode placement caused some differences in recordings and the best recording was obtained when the active electrodes were placed over the middle of the SCM muscle. Patko et al. claimed that a 500-Hz Short Tone Burst (STB) signal was more effective compared to a click stimulus in evaluating the sacculocolic pathway [22].

Murofishi et al. reported that a VEMP response could be obtained both with a click stimulus and a short tone stimulus [23]. Akin et al. observed a significant difference in favor of the tone burst stimulus when they compared a click stimulus and a tone-burst stimulus in terms of latency and amplitude. Similarly, some other studies also reported findings in favor of tone-burst stimulus. It should be mentioned that the parameters used in the present study show a similarity to the parameters used by Akin et al. and Petrak.

Various studies reported that the best VEMP latencies would be observed when a stimulus having a stimulation level of 95 dB nHL was used [21,23]. In our study, a VEMP response was obtained at 90 dB nHL in all the participants.

In the literature, the findings on VEMP differ. It should be taken into consideration that this difference could be related with the test parameters used. In order to use a test in a differential diagnosis, the application and evaluation parameters should be standard and sufficient data should be collected on the normal population.

Behçet's syndrome is characterized by recurrent oral aphthae and any of several systemic manifestations including genital aphthae, ocular disease, skin lesions, gastrointestinal involvement, neurologic disease, vascular disease, or arthritis. Behçet's may have been described by Hippocrates, but it was brought to the attention of the modern medical community by Hulusi Behçet in 1937 [24,25].

Among some populations, there may be differences in the frequencies or types of certain manifestations, including neurologic disease [26].

The International Criteria for Behçet's disease (ICBD) were developed in 2006 in an effort to improve sensitivity compared with the ISG criteria, but they are not widely accepted [27]. Each of several findings is assigned a point value; the criteria require a total of at least three points for diagnosis of Behçet's:

Genital aphthosis – Two points

Ocular lesions (anterior uveitis, posterior uveitis, or retinal vasculitis) – Two points

Oral aphthosis – One point

Skin lesions (pseudofolliculitis or erythema nodosum) – One point

Vascular lesions (superficial phlebitis, deep vein thrombosis, large vein thrombosis, arterial thrombosis, or aneurysm) – One point

Pathergy – One point

Validation studies have estimated a sensitivity of 87 to 96.5 percent, a specificity of 88.9 to 97.3 percent, and an accuracy of 74.2 to 85.5 percent for these criteria [28].

Conclusion

ASSR yields some information on the hearing level in patients having Behcet's disease. However, there is a weak correlation between ASSR and pure tone thresholds, and its reliability in predicting auditory brainstem responses is not high.

Moreover, the VEMP test should not be used in the differential diagnoses in patients having Behcet's disease. Further studies on larger cohorts are required to establish the related standards for both the ASSR test and the VEMP test.

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