

Evaluation of the Effect of Behçet's Disease on Vestibulo-Ocular Reflex with Video Head Impulse Test

Behçet Hastalığının Vestibulo-Oküler Refleks Üzerine Etkisinin Video Baş Savurma Testi ile Değerlendirilmesi

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ABSTRACT Objective: Behçet's disease (BD) is characterized by recurrent oral and genital ulcers, uveitis and vasculitis throughout the body. There are not many studies in the literature on the involvement of the vestibular system in BD. Our aim is to evaluate the vestibular system in Behçet's patients and to determine the clinical importance of video head impulse test (vHIT). **Material and Methods:** Twenty patients (11 females and nine males) with BD and 15 healthy volunteers (seven females and eight males) were included in the study. Pure tone audiometry (PTA), videonystagmography (VNG), dizziness handicap inventory (DHI) and vHIT tests were administered to all individuals. Data were evaluated by statistical methods. **Results:** The mean age of the patients with BD was 44±11.2 years, and the mean age of the healthy volunteers was 42±13.3 years. The DHI scores of the patient group were higher than the control group. Results of vHIT showed significantly lower VOR gain in the left lateral, right, and left posterior semicircular canals in the BD group compared to the control group. Nine (45%) of the BD patients had overt saccade, but none had covert saccade. Overt and covert saccade were not observed in the healthy volunteers. **Conclusion:** vHIT is a fast and accurate test that can be used to evaluate the vestibular system in patients with BD.

Keywords: Behçet's disease; vestibulo-ocular reflex; video head impulse test; oral ulcers; genital ulcers; vasculitis

ÖZET Amaç: Behçet hastalığı (BD), vücutta tekrarlayan oral ve genital ülserler, üveit ve vaskülit ile karakterizedir. Literatürde vestibüler sistemin BD'ye katılımı ile ilgili çok fazla çalışma yoktur. Amacımız Behçet hastalarında vestibüler sistemi değerlendirmek ve video baş savurma testinin (vHIT) klinik önemini belirlemektir. **Gereç ve Yöntemler:** Yirmi iki hasta (11 kadın ve 9 erkek) BD ve 15 sağlıklı gönüllü (7 kadın ve 8 erkek) çalışmaya dahil edildi. Tüm bireylere saf ton odometri (PTA), videonistagmografi (VNG), baş dönmesi handicap envanteri (DHI) ve vHIT testleri uygulandı. Veriler istatistiksel yöntemlerle değerlendirildi. **Bulgular:** Behçet Hastalığı olanların yaş ortalaması 44±11,2, sağlıklı gönüllülerin yaş ortalaması 42±13,3 idi. Hasta grubunun DHI skorları kontrol grubundan daha yüksekti. vHIT sonuçları BD grubunda sol lateral, sağ ve sol arka semisirküler kanallarda kontrol grubuna göre anlamlı derecede düşük vestibüler oküler refleks (VOR) artışı gösterdi. Behçet hastalarının 9 (%45)'unda açık seğirme vardı, ancak hiçbirinde örtülü seğirme yoktu. Sağlıklı gönüllülerde açık ve örtülü seğirme görülmedi. Behçetli hastalarda VOR'un etkilendiği bulundu. **Sonuç:** vHIT, BD'li hastalarda vestibüler sistemi değerlendirmek için kullanılabilecek kolay, hızlı ve güvenilir bir testtir.

Anahtar Kelimeler: Behçet hastalığı; vestibulo-oküler refleks; video baş savurma testi; oral ülserler; genital ülserler; vaskülit

Behçet's disease (BD) is a chronic recurrent vasculitis that affects the small vessels of almost all organs with unknown etiology.¹ The prevalence in Turkey is 20 to 420/100.000.² It is usually seen in the third decade of life and the average age of onset in

Turkish patients was reported to be 23.3 years.³⁻⁵ It is more common in men than in women. The underlying histopathological findings include leukocytoclastic vasculitis, fibrinoid necrosis of the postcapillary venules and perivascular neutrophilic accumulations.

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Apart from oral and genital ulcers, neurological, gastrointestinal, vascular, cardiac, pleuro-pulmonary and testicular involvements may be observed.^{6,7} It affects all systems in the body, including the audiovestibular system. Hearing loss, dizziness and vertigo can be seen in Behçet' disease.^{8,9}

The International Clinical Criteria for Behçet's Disease classification states patients must present: (a) Recurrent oral ulcerations (aphthous or herpetiform) at least three times in one year and (b) any two of the following: - Recurrent genital ulcerations, -Eye lesions (uveitis or retinal vasculitis) observed by an ophthalmologist, -Skin lesions (erythema nodosum, pseudo-folliculitis, papulo-pustular lesions, acneiform nodules) unable to resolve with corticosteroids or -positive pathergy test read by a physician within 24-48 hours.¹⁰

The video head impulse test (vHIT) is an instrumented bedside technique used to diagnose reduction in vestibular function in one ear compared to the other. All of the three semicircular canals in the vestibular system and the superior and inferior branches of the vestibular nerve are evaluated. Basically, the test incorporates a new technology that uses a high speed, lightweight video goggle to measure eye velocity and record "catch up" saccades in patients with impaired vestibular ocular reflex (VOR) function. vHIT provides a quick and objective measure of the VOR in response to head movements in the natural range of daily motions.

In this study, we aimed to evaluate the vestibular system involvement of BD using vHIT which presents accurate and fast diagnosis of the vestibular system involvement.

MATERIAL AND METHODS

Twenty (N: 9 males 45%, 11 females 55%) cases who were complaining of dizziness and being monitored with the diagnosis of Behçet's disease for at least three years in our hospital (Physical therapy and rehabilitation) were designed as the study group. They were sent to neurology and ENT because of dizziness. All BD cases were being followed by the same neurologist and were assured not to have neuro-Behçet. Fifteen healthy individuals (N: 8 males 53.3%, 7 females 46.7%) were designed as the con-

trol. The approval of the local Ethics Committee of Okmeydanı Research and Education Hospital was taken with the project number: 48670771-514.10. Informed consent was obtained from the participants.

All cases received a detailed otolaryngologic examination and had normal otoscopic findings. The control group did not have any kind of neurological, otologic or vestibular symptoms.

Exclusion criteria were pediatric age group, sight-loss, limited neck motion that lacks focusing in the test, on-going vestibular rehabilitation patients, neuro-Behçet's disease involving the central nervous system and being under vestibular suppressant medications.

The vestibular status of the participants were examined by the Turkish version of the Dizziness handicap inventory (DHI-TR). This is one of the disease specific questionnaire developed for individuals with dizziness or balance problems in order to determine how vertigo or disequilibrium affect individual's quality of life and composed of physical, functional and emotional domains.

Each participant underwent pure tone audiometry (PTA) to detect any disorder through the frequencies between 250-8000 Hz (Interacoustics AC-40, Denmark).

Finally, videonystagmography (VNG) and vHIT tests were performed by ICS Impulse video glasses system (GN Otometrics, Schaumburg, IL, USA).

VHIT protocol: The participants were seated in a well lit room at a distance of 1 m from a target point on the wall approximately 90 cm above the floor. A pair of glasses with a high frequency (250 Hz) video camera was positioned to record real-time eye movements. There was a motion sensor to measure head movements. Before each test, calibration was performed to ensure correct measurement. All tests were performed by a single experienced nurse. The head impulses were delivered unpredictably. This was required both in regard to direction and timing. The head impulses were applied with a small amplitude (5° - 20°) and high acceleration ($1,000^{\circ}/s^2$ - $4,000^{\circ}/s^2$). To perform horizontal semicircular canal testing, the head of the participant was turned away from the center to the right or left sides and a minimum of 10 head

impulses were delivered to each side. To perform vertical semicircular canal testing, the hands of the attendant were placed on top of the patient's head and the fingers were directed in the direction of the anterior semicircular canal to be tested. For the left anterior and right posterior semicircular canals, the head was rotated to right and a down movement was applied to the head to stimulate the canals. For the right anterior and left posterior semicircular canals, the head was rotated to left and a down movement was applied to the head to stimulate the canals. VOR saccades of the patient were recorded and transferred to a computer. Corrective saccades are defined as transient (fast) eye movements. Corrective saccades that occur after the head rotation were referred to as overt saccades whereas corrective saccades that occur during the head rotation were referred to as covert saccades.

Statistical analysis were done by SPSS-22 (IBM, Turkey). The normality of the data distribution was assessed using the Shapiro-Wilks test. Student's t-test was used for between-group comparisons of normally distributed parameters, and the Mann-Whitney U test was applied to compare parameters that were not normally distributed. Descriptive statistics included means, standard deviations, and frequencies. A *p*-value lower than 0.05 was accepted as statistical significant.

RESULTS

The mean age of the patients with BD was 44±11.2 years, and the mean age of the healthy volunteers was 42±13.3 old. Twenty patients with BD (N: 9 males

45%, 11 females 55%) and 15 healthy individuals (N: 8 males 53.3%, 7 females 46.7%).

There was no statistical difference in age and gender between the BD and control groups.

In BD group, four cases had sensorineural hearing loss (SNHL) in all frequencies (500–8000 Hz). The high frequencies (4000, 6000, and 8000 Hz) revealed bilateral loss of 25 dB or more in sixteen BD cases. In the control group, four cases had high frequency sensorineural hearing loss. The DHI scores were 21.40±7.8 in BD and 1.60±1.5 in the control group. The results of BD were significantly higher (*p*<0.001). VNG tests were normal in all subjects. No spontaneous or positional nystagmus were detected.

According to vHIT results, the average VOR gain of the left anterior semicircular canal of BD was 0.64 (range: 0.25-0.80) and was significant compared to the gain of the control group which was 0.82 (range: 0.71-0.90) (*p*<0.05). The average VOR gain of the right posterior semicircular canal of BD was 0.65 (range: 0.41-0.82) and was significant compared to the gain of the control group which was 0.80 (range: 0.72-0.90) (*p*<0.05). The average VOR gain of the left posterior semicircular canal of BD was 0.74 (range: 0.19-0.99) and was significant compared to the gain of the control group which was 0.81 (range: 0.75-0.95) (*p*<0.05). VOR gains of the other canals compared to the control group were deemed normal (Table 1, Figure 1, Figure 2).

In nine (45%) of the patients with BD, overt saccade was present but no covert saccade was observed.

TABLE 1: VOR Gains of the semicircular canals.

	Groups				<i>p</i>
	BD (n=20)		Control (n=15)		
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	
LL	0.92±0.10	0.91 (0.78-1.12)	0.90±0.06	0.88(0.82-1.04)	0.653 ^a
RL	1.01±0.13	0.98 (0.86-1.33)	1.01±0.10	0.95(0.92-1.16)	0.805 ^b
LA	0.60±0.15	0.64 (0.25-0.80)	0.81±0.06	0.82(0.71-0.90)	≤ 0.001 ^{a*}
RP	0.64±0.10	0.65 (0.41-0.82)	0.80±0.07	0.80(0.72-0.90)	≤ 0.001 ^{a*}
LP	0.68±0.19	0.74 (0.19-0.99)	0.84±0.07	0.81(0.75-0.95)	0.003 ^{b*}
RA	0.81±0.18	0.79 (0.54-1.18)	0.90±0.10	0.90(0.78-1.02)	0.088 ^a

*: *p*<0.05

a: independent sample t-test, b: Mann-whitney U test, BD: Behçet's disease; SD: standard deviation, LL: Left lateral semicircular canal, RL: Right lateral semicircular canal, LA: Left anterior semicircular canal, RA: Right anterior semicircular canal, LP: Left posterior semicircular canal, RP: Right posterior semicircular canal.

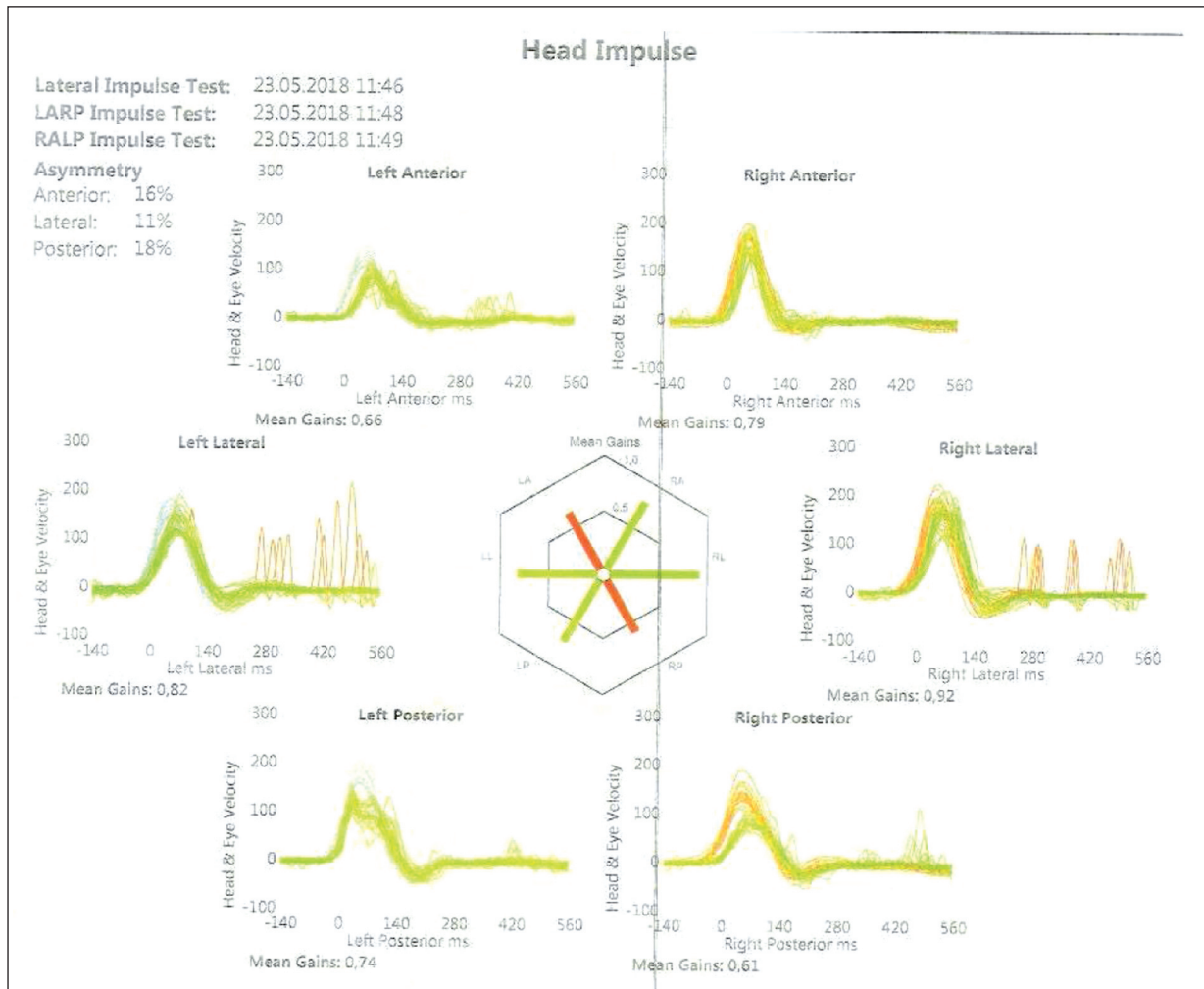


FIGURE 1: Video head impulse test example of a patient (presence of overt saccades and decreased gain levels on left anterior and right posterior semicircular canal).

Overt and covert saccade were not present in all of the healthy volunteers (Table 2).

DISCUSSION

BD is a chronic inflammatory vasculitis involving small vessels with unknown etiopathogenesis. HLA-B5 and HLA-DR5 are associated with alloantigens. This autoimmune disease can be familial and has a genetic basis.¹¹ Although BD is characterized by the triad of severe uveit, along with oral and genital aphthous ulcers due to small vessel vasculitis, it may affect all systems in the body, including the audiovestibular system.

The arterial blood supply to the cochlea and vestibular structures is provided by the branches of

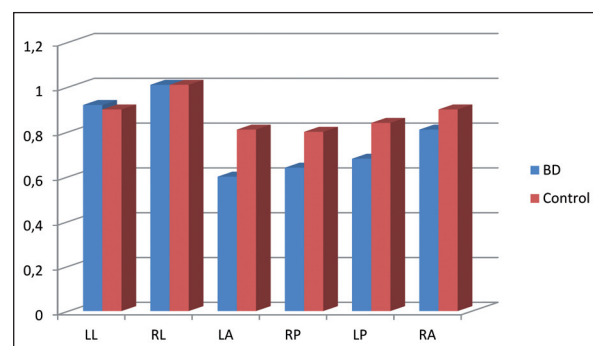


FIGURE 2: VOR gains of the semicircular canals.

the labyrinthine artery, the common cochlear artery and the anterior vestibular artery. Vasculitis may damage these branches in BD.¹²

TABLE 2: VOR Gains of the semicircular canals.

	Groups				
	BD		Control		
	n	%	n	%	
Gender	M	9	45,0	8	53,3
	F	11	55,0	7	46,7
Age(mean)			44±11,2		42±13,3
OVERT	+	9	45,0	0	0,0
	-	11	55,0	15	100,0
COVERT	+	0	0,0	0	0,0
	-	20	100,0	15	100,0

SD: standard deviation.

Based on this hypothesis, labyrinthine artery involvement in BD is of utmost importance. Due to the anatomical nature of humans, cochlea and vestibular structures have a very limited blood supply. The objective findings of the involvement of the cochlea and horizontal semicircular canals in the current study may lead to unpredictable or asymmetrical involvement of the semicircular canals.

Otologic and vestibular involvement rates in BD are variable in the literature. Alajouanine et al. showed the audiovestibular involvement in BD in 1961.¹³ Brahma et al. identified abnormalities of auditory and vestibular system in 62% and 37% of patients respectively, whereas Pollak et al. found auditory and vestibular abnormalities in 73% and 54% of patients, respectively.^{8,9} These findings obviously support that the cochlear involvement was greater than vestibular involvement. Peripheral involvement of the audiovestibular system was seen more than central involvement, and there was no relationship with other organ involvement, duration of disease, age or gender.⁹

Morales-Angulo et al. assessed otorhinolaryngological problems in 33 BD and reported audiovestibular manifestations in six of them.¹⁴ In BD, hearing loss was usually bilateral and at high frequencies. Our study revealed four cases with SNHL in all frequencies whereas at the higher frequencies (4000, 6000, and 8000 Hz), there was bilateral loss of 25 dB or more in 16 BD patients.

VNG and caloric tests were being used to evaluate the vestibular system in patients with BD.^{9,15} In

Külahlı's study, the caloric test was normal in all 62 patients with BD, while in 21 patients, hypometric or hypermetric saccades were found.¹⁵ In Pollak's study, canal paresis and peripheral spontaneous nystagmus in the caloric test were found in four of 26 BD patients and saccadic pursuit in two patients. We used VNG to differentiate central pathologies and peripheral positional vertigo. In none of our patients, we detected pathology in gaze, saccades and tracking. The caloric test is limited in how much of the vestibular system it tests: the stimulation primarily tests only the lateral semicircular canal at very low frequencies. The video head impulse test (v-HIT) was proposed to indicate the status of the VOR at high frequencies in all semicircular canals at the same time. Our results, however were not in concordance with the published data; we included BD cases without central involvement which is why our results were contradictory.

Choung et al. reported spontaneous nystagmus in two, saccade in one, and canal paresis in five cases with BD.¹⁶ Sixteen cases had audiologic or vestibular disorders. They reported that the inner ear involvement of all BD patients should be evaluated and audiometry and positive vestibular function tests might be helpful in the diagnosis and management of BD.

Erbek et al. conducted a study of 26 patients with BD.¹⁷ In the caloric test, four (15.3%) patients were found to have canal paresis. Cervical vestibular evoked myogenic potential (cVEMP) detected prolongation of P13-N23 latencies. Seven patients had a delayed cVEMP response. They reported that au-

diovestibular dysfunction was not uncommon in patients with BD. Bayram et al. also found abnormal cVEMP findings in their study, while oVEMP did not detect any pathology.¹⁸

The head impulse test was described by Halmagyi and Curthoys in 1988 vHIT is a test that measures eye speed with light camera glasses and captures saccades when high-speed head movements are affected by impaired VOR functions.^{19,20} In a short time, VOR was evaluated at high frequencies for all semicircular canals.^{21,22}

A study by Ertugrul et al. used vHIT to evaluate 31 BD cases.²³ They performed PTA, vHIT, post-head shake nystagmus test (PHSNT), and dizziness handicap inventory (DHI) to check for audiovestibular system involvement. Saccades were detected only in the horizontal semicircular canals. The VOR gain was significantly lower in the BD group than in the control group. DHI scores were higher in the BD group than in the control group. There was no correlation between duration of disease and saccade detection. In our study, the VOR gain in the left lateral, right, and left posterior canals of BD patients were significantly lower than the control group. This may be because vasculitis affects the feeding of different canals. Nine (45%) cases had overt saccade and there was no covert saccade. These findings indicate that the audiovestibular system was involved in BD and vHIT was useful in evaluating the vestibular system. Our study evaluated the vestibular system with VNG and vHIT in BD and it is the second study using vHIT.

We, however have a limitation in our study; patient population was low. We believe, future studies can be conducted in larger groups.

CONCLUSION

The published data reveals VNG, VEMP have been used to evaluate the vestibular system in BD. We tested all of the semicircular canals simultaneously using vHIT and found a decrease in VOR gain and presence of overt saccades in some canals. These findings suggest that the vestibular system is frequently affected in BD without Neuro-Behçet.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Belgin Tutar; **Design:** Güler Berkiten; **Control/Supervision:** Onur Akan; **Data Collection and/or Processing:** Semih Karaketir, Ömür Biltekin Tuna; **Analysis and/or Interpretation:** Yavuz Uyar; **Literature Review:** Belgin Tutar; **Writing the Article:** Belgin Tutar; **Critical Review: References and Fundings:** Güler Berkiten.

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