P50 variations in Behçet's patients without neurologic findings

Meral Aşçioğlu, *PhD,* ***Mustafa Arslan,*** *MD,* ***Cem Süer,*** *MD,* ***Özcan Aşçioğlu,*** *MD,* ***Çiğdem Özesmi,*** *PhD,* ***Murat Borlu,*** *MD,* ***Abdülhakim Coşkun,*** *MD,* ***Ali S. Gönül,*** *MD,* ***Emel Köseoğlu,*** *MD.*

ABSTRACT

Objective: In the present study, subclinical lesion involvement was investigated using the P50 component in Behçet's patients without neurological manifestation.

Methods: We performed this clinical research in Erciyes University, Faculty of Medicine between December 2000 and November 2001. The studies were carried out on 18 Behçet's patients without neurologic findings and 18 volunteers for control. Standard Ag/AgCl electrodes in plastic cups were used for monopolar EEG derivations. They were attached with electrode paste and tape at the Cz (vertex) according to the 10-20 system. The auditory stimuli were delivered in pairs. The P50 waves, which may be taken from approximately 50 msec from the stimuli, were collected by computer system. Amplitudes and latencies of the P50 components were measured in the same system.

Results: This study showed that the suppression of P50 responses performed by the test stimuli, was significantly more decreased in Behçet's patients than the control subjects.

Conclusion: The decrease of the suppression of the auditory P50 response to repeated stimuli reflects a deficit in the central nervous system's ability, such as attention, cognition, and sensory input in Behçet's patients and can be used as a neurophysiological marker in subclinical lesions in these patients.

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From the Departments of Physiology (Aşçioğlu M, Arslan, Süer, Özesmi), Dermatology (Aşçioğlu O, Borlu), Radiology (Coşkun), Psychiatry (Gönül), and Neurology (Köseoğlu), Faculty of Medicine, University of Erciyes, Kayseri, Turkey.

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Address correspondence and reprint request to: Dr. Mustafa Arslan, Department of Physiology, Faculty of Medicine, University of Erciyes, Kayseri, 48. Sokak, Seda Apartmanı, 24/17 Yenimahalle-Kirikkale, Turkey. Tel. +90 (318) 2120526. E-mail: marslan36@yahoo.com / marslan36@hotmail.com

Behçet's disease is a multisystem disorder, which was first described in 1937 by a Turkish dermatologist, Hulusi Behçet as a triad of aphthous lesions of the oral mucosa, genital ulcerations, and hypopyon iritis.[1] The disease is often a progressive disorder, and includes neurologic manifestations such as meningoencephalitis, aseptic meningitis, seizures, bulbar and pseudobulbar palsy, pyramidal tract abnormality, cerebellar ataxia, emotional incontinence, subcortical dementia, transient ischemic attacks, stroke, and pseudomotor cerebri.[2] It has a world-wide distribution, but is most common in the Pacific rim and the Eastern Mediterranean.[3] At present, there are no laboratory markers that correlate well with the clinical activity in Behçet's disease.[4] In previous studies, abnormal brainstem auditory evoked potential (BAEP), visual evoked potential (VEP), P300, and single-photon emission computed tomography (SPECT) findings were reported in some patients with Behcet's disease without neurologic manifestation even with negative findings on brain MRI.[2,5] Evoked potential components such as P50, P1, N1, P2, N2, and P3 have been used to investigate the effects of various physiological events and some drugs on cognitive functions.[6,7] These components reflect CNS functions and neural events that are related to transient sensory and task-relevant cognitive or motor events and provide information on different aspects of cognition such as, attention and stimulus evaluation and response preparation execution.[8,9] The middle latency auditory evoked potential contains a component of P50 with a fronto-central positive topographic distribution that occurs approximately 50 ms after a click stimulus. When paired click stimuli (conditioning and testing) are presented, the second stimulus usually evokes a P50 wave that is inhibited or gated by the effect of the first stimulus.[10-12] The P50 suppression is an operational measure of sensory gating that can be assessed by averaging electroencephalographic responses to multiple pairs of auditory clicks separated by 500 msec.[13] Sensory gating can be operationalized as the percentage decrease in the P50 amplitude from the first to the second click. Whereas healthy subjects show a significant decrement from the first to the second P50, patients with schizophrenia often do not.[13] Deficient sensory gating has also been reported in marijuana users,[14] in patients with chronic post-traumatic stress disorder,[15] after traumatic brain injury,[16] in

healthy persons after administration of amphetamine,[17] Alzheimer's disease,[18] and, migraine patients.[19] This suppression of the auditory P50 response to repeated stimuli reflects the CNS ability to screen out repetitive stimuli,[15] and measures such as P50 suppression are used to study cognitive and attentional dysfunction among these patients.[12,15] However, P50 suppression in Behçet's patients has seldom been studied. It is important therefore, to evaluate the suppression of P50 in Behçet's patients. The aim of the present study was to assess whether the P50 component can be used as a neurophysiological marker of subclinic lesions in Behçet's disease.

Methods. This clinical research was performed in Erciyes University Faculty of Medicine between December 2000 and November 2001. Eighteen Behcet's disease patients (25-45 years old, mean ± SD = 36.2 ± 7.2 years) without neurologic findings, and 18 healthy volunteers (21-44 years old, mean ± SD = 33.6 ± 7.3 years) were accepted for the study. The study was approved by the Ethics Committee of Erciyes University Medical School, and all patients gave written informed consent. Prior to recordings the people in the study were subjected to psychiatric, neurologic findings such as meningoencephalitis, aseptic meningitis, seizures, bulbar and pseudobulbar palsy, pyramidal tract abnormality, cerebellar ataxia, emotional incontinence, subcortical dementia, transient ischemic attacks, stroke and pseudomotor cerebri, and radiologic examination, and also, they were asked to refrain from alcohol, caffeine, and other drugs for at least 4 days.[20] Subjects were relaxed, awake, and seated upright with eyes open in an acoustically isolated room during the recording session. Standard Ag/AgCl electrodes in plastic cups were used for monopolar EEG derivations. They were attached with electrode paste and tape at Cz (vertex) according to the International 10-20 system. Linked right ear electrodes were used as inactive references and the ground electrode was attached to the left earlobe. Electrode resistance was less than 10 kohm. The signals from the electrodes were amplified and filtered by Nihon Kohden amplifier (AB-621G), and sent to analogue inputs of a pentium 100 computer for on-line analogue-digital conversion. Sampling rate was 1000 Hz. The electrooculogram (EOG) from the superior orbital references to the lateral canthus was also recorded. Individual trials were rejected if the EOG and EEG activity was greater than 50 μV, which indicates movement artifact. Auditory stimuli were presented in pairs in a conditioning-testing (C-T) design with a 0.5 second interpair interval and a 10 second interstimulus interval by the Brain Data Acquisition System, and were delivered through a headphone. Peak intensity was 70 dB sound-pressure level. Each average consisted of the responses to 32 pairs of stimuli.[21] Data were collected for 100 msec following the click stimulus for all the interpair intervals. The C-T protocols lasted approximately 6 minutes each, during which our subjects were instructed to keep their eyes open and still. Subjects were monitored by the technician via video camera throughout the recording session. Thirty-two pairs of responses were averaged off-line, over 100 ms epochs with 2 msec pre stimulus baseline. The P50 response data were analyzed as follows. Averaged evoked potentials were measured for peak amplitude of the P50 wave. The conditioning P50 wave (C) was defined as the maximal positive activity occurring between 40-80 msec after the stimulus. If more than one peak was identified, the later one was selected. The amplitude was measured relative to the baseline. The test P50 wave (T) was identified as the most positive peak with a latency from the test stimulus within 10 msec of the latency of the conditioning P50 response. If there were no peak in that range, the amplitude was noted as zero. Conditioning-testing ratio (C/T ratio) was expressed as a percentage, the amplitude of the test P50 wave was divided by the amplitude of the conditioning P50 wave and multiplied by 100. Statistical analysis was computer processed (SPSS version 11.0.5 for Windows, Chicago, IL, USA). *P*-values <0.05 were considered significant. The results of the study were expressed as mean ± SD. The data were analyzed statistically by Student's t-test.

Results. In the statistical comparison between groups in terms of age, body weight, height, ASA group, gender, duration of operation and anesthesia, no statistically significant difference was found (**Table 1**) (p>0.05). As shown in **Table 2**, Behçet's patients had a

Table 1 - Demographic variables (mean ± SD).

Characteristics	Healthy control subjects (n=18)	Behçet's patients (n=18)	p
Age (year)	33.6 ± 7.3	36.2 ± 7.2	0.620
Weight (kg)	65.6 ± 10.5	64.7 ± 9.2	0.636
Height (cm)	162.7 ± 6.3	161.9 ± 5.5	0.890
Gender (Female/Male)	9:9	10:8	0.796

Table 2 - P50 amplitudes, latencies and C-T ratios in Behçet's patients and healthy control subjects (mean ± SD).

Parameters	Healthy control subjects (n=18)	Behçet's patients (n=18)	p
C amplitude (mV)	3.28 ± 1.12	3.14 ±.1.04	0.694
T amplitude (mV)	1.13 ± 0.65	1.87 ± 0.69*	0.020
Latency (ms)	55.18 ± 11.82	55.55 ± 12.75	0.855
C/T ratio (%)	36.94 ± 19.41	60.73 ± 16.69*	0.002

C amplitude - Conditioning P50 wave, T amplitude - Test P50 wave, C/T ratio- Conditioning-testing ratio
*p<0.05 - compared to healthy control subjects

P50 suppression that was significantly more decreased than the healthy control subjects. The conditioning and test P50 amplitudes, test P50 latencies and C/T ratios in both groups are compared in **Table 2.** Statistical analyses found a significant decrease in Behçet's patients compared with the healthy control subjects (p=0.020), while there were no significant differences between peak latency values of the 2 groups (p>0.05), and also Behçet's patients had a C/T ratio (%) that was significantly higher than the determined value of healthy subjects (p=0.002), (**Table 2**).

Discussion. In previous studies, abnormal BAEP, VEP, P300, and SPECT findings were reported in some patients with Behcet's disease without neurologic manifestations,[2,5,22] and these studies have also reported that evoke potentials studies in Behçet's disease might be helpful to separate neuro-Behçet's from other disorders with similar symptomatology,[13] to disclose subclinical CNS involvement,[20] to evaluate and monitor CNS disease activity, and to provide objective measures of treatment response.[2,5,22] However, none of these studies investigated whether auditory P50 can be used as a neurophysiological marker in subclinic lesions in Behçet's patients. In the present study, subclinical involvement was investigated by using P50 in Behçet's patients without neurological manifestations. When the results of this study were evaluated in the light of the knowledge in the current literature,[23] it was concluded that the decrease of suppression of P50 responses in Behcet's patients without neurologic findings may be related to impaired neuronal activity due to cerebral small blood vessel vasculitis and deficiency in associated neurotransmitters or receptor systems. Also, it has been reported that sensory gating abnormalities had been shown in some disorders related to neurotransmitter deficiency or receptor pathologies.[24]

In summary, our results indicate that the decrease of suppression of P50 responses in Behçet's disease patients without neurologic findings may reflect subclinical neurologic involvement and may aid to diagnose neuro-Behçet's diseases at an early stage of involvement.

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