Aggression and the Event-Related Potentials in Antisocial Personality Disorder

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ÖZET:
Antisosyal kişilik bozukluklarında olaya ilişkin potansiyeller ve saldırganlık

Amaç: Bu çalışmada, antisosyal kişilik bozukluğu (ASKB) olan ve alkol madde etkisinden arındırılmış bir erkek örnekleminde olaya ilişkin potansiyellerin (ERPs) kontrol grubu ile karşılaştırılması, ayrıca ERPs ve saldırganlık arasında ilişkinin olup olmadığının belirlenmesi amaçlanmıştır.
Yöntem: 42 ASKB'li birey ve kontrol grubu olarak da 44 sağlıklı birey çalışmaya dâhil edildi. Her iki grupta bulunan denekler çalışmaya katılmadan en az 15 gün önce alkol ve madde kullanımını kesmişti.
Bulgular: Yaş, medeni durum, eğitim düzeyleri açısından gruplar arasında anlamlı fark yoktu. P3 (LP3) latansı ASKB grubu ve kontrol grubu arasında anlamlı fark göstermedi. P3 Amplitüd (AP3) değerleri ASKB grubunda kontrol grubuna göre anlamlı oranda düşük bulundu($p < 0.01$). N2 latansı (LN2), LP3, N2 amplitüdü (AN2), AP3 değerleri ile Buss-Perry Saldırganlık Ölçeği toplam ve alt ölçek puanları arasında her iki grupta da korelasyon yoktu.
Sonuç: Antisosyal grupta AP3'ün anlamlı olarak azalmış olması literatürle uyumludur. Literatürden farklı olarak LP3'ün gruplar arasında anlamlı farklılık göstermemesi dikkate değer bir sonuçtur.

Anahtar sözcükler: Antisosyal kişilik bozukluğu, saldırgan davranış, olaya ilişkin potansiyeller

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ABSTRACT:
Aggression and the event-related potentials in antisocial personality disorder

Objective: In this study, we measured event related potentials (ERPs) in a male sample of antisocial personality disorder (ASPD) patients who were free of substance and alcohol abuse and compared them with those of normal subjects. We also aimed to determine whether or not there was a correlation between aggressive behaviors and ERPs .
Materials and Method: A total of 42 ASPD patients and a control group of 44 healthy subjects were enrolled in the study. In both groups, the subjects had not used alcohol or any psychotropic medicine for at least 15 days prior to enrollment.
Results: There were no significant differences in age, education, and marital status between the ASPD and control group. P3 amplitude (AP3) values were significantly lower in the ASPD group compared to the controls ($p < 0.01$). P3 latencies (LP3) were no different in the ASPD group relative to the controls. No correlation was found between the N2 latencies (LN2), LP3, N2 amplitude (AN2) or AP3 values, and the total and subscale scores of the Buss-Perry Aggression Questionnaire in either group.
Conclusion: AP3 in the antisocial group was reduced significantly compared to the control group in line with previous literature reports. In contrast to the literature, LP3 did not show significant differences between the groups, which is a noteworthy result.

Key words: Antisocial personality disorder, aggressive behavior, event related potentials

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INTRODUCTION

Aggressive behavior generally has a target which is described as anger, rage or hostility. The content of aggressive behavior consists of objection, fear, anger, impulsiveness and violence (1). Some authors have suggested that the biological origin of aggressive behavior is based on brain injury. While damage in the prefrontal areas causes a lack of behavioral control, subjects with lesions in the medial and frontal areas develop many psychiatric symptoms including aggressive behavior and social incompatibility (2,3). Although it is observed in the normal population and accompanies many psychiatric and neurological diseases, aggressiveness is an important issue commonly seen in personality disorders, particularly in ASPD (4,5,6). Evidence concerning the neurobiological basis of aggressive behavior has been increasing rapidly. Neurophysiological studies investigating the biological framework of aggressiveness have recently focused on EEG and ERPs (7). Evoked potentials (EP) have been used to record the electrophysiological response of the central nervous system to external stimuli. In clinical practice, short-latency brainstem auditory evoked potential (BAEP), somatosensory evoked potential (SEP) and visual evoked potential (VEP) are used to reflect the neuronal response to the delivered stimuli. Amplitude and

latencies of the EP depend on the physical characteristics of the stimulus. Therefore "stimulus-related potentials" (SRPs) are independent of the subject's attention or interest; however, "event related potentials" (ERPs) which represent an EP, occur by neuroelectric response to external stimuli. Occurring as a series of positive and negative peaks, the presence of various amplitudes, latencyies durations, and topographies of ERPs are considered as reliable indicators for cognitive and psychological processes (8,9,10).

The N2 component of the ERP, that occurs approximately 200-250 milliseconds after the stimulus delivery in various tasks, reflects a decision process which controls behavioral responses in sensory discrimination tasks (11).

P3 is a positive component which occurs approximately 300 milliseconds after the stimulus delivery. It occurs during selective attention or a discrimination task, regardless of the stimulus features (12). P3 is considered as a cognitive neuroelectrical phenomenon.

Since they represent a noninvasive technique providing information about neuronal activity, ERPs have been studied in various psychiatric disorders. The N2 and P3 components have been used in many studies investigating the neurophysiology causes of aggressive behavior. Bond and Surguy (2000) suggested that a reduced AP3 could be an indicator of violent behavior and aggressiveness (13). The results of a study in which visual P3 was measured in college students, indicated a significantly reduced P3 amplitude and a prolonged latency for impulsive aggressive subjects (14). In their study, Kiehl et al. (2006) demonstrated an increased AN2 and a reduced AP3 in psychopathic subjects (15).

Literature data support the theory that antisocial personality behavior is associated with a reduced P3 amplitude, although the findings of the study conducted by Raine et al. in 1987 demonstrated the opposite (16).

Since antisocial personality disorder (ASPD) and substance abuse demonstrate a very high rate of co-morbidity, the reliability of studies in this area is not satisfactory. Our study sample is relatively free of substance abuse because our subjects were drawn from a military population. The present study was designed to measure ERPs and compare them between a normal population and ASPD subjects free from substance abuse and psychotropic medicine use. In addition, the study aimed to investigate whether there was an association between aggressiveness and the components of ERPs.

MATERIALS AND METHOD

Subjects

This crossover case-control study was conducted at Gülhane Military Medical Hospital in collaboration with the Psychiatry Department and the Electrophysiology Laboratory of the Neurology Department. The study subjects were selected from the patients presenting to the outpatient Mental Health and Disorders Clinic between April 2004 and August 2004. Study subjects consisted of consecutive patients diagnosed with ASPD by a psychiatrist using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-

Table 1: The distribution of the excluded participants

Control Group	N	The Experimental Group	N
Depressive disorder	2	Depressive disorder	3
Panic disorder	1	Psychotic disorder	1
Conversion disorder	1	Borderline personality disorder	3
Obsessive compulsive disorder	1	Substance/Alcohol addiction+ withdrawal symptoms	4
Hepatitis B + Interferon treatment	1	Attention deficiency and hyperactivity disorder	1
Bronchial asthma	1	Post traumatic stress disorder	2
Reluctant participants	5	Dissociative disorder, NOS (Not otherwise specified)	1
Inadaptable participants	2	Organic amnestic disorder	1
		Epilepsy	1
		Participants who had taken drugs in the last 15 days	2
		Reluctant to participate	9
		Inadaptable participants	4
Total	14	Total	32

II). In the enrollment period, 74 subjects were interviewed and 42 young males meeting the inclusion criteria were enrolled. For the control group, a total of 58 young male healthy volunteers were interviewed and 44 healthy volunteers meeting the inclusion criteria, matched by age and education were enrolled.

Subjects with any DSM-IV Axis I disorder, substance dependence, convulsions, central nervous system disease, metabolic disorder or mental retardation were excluded from the study (Table 1). The study subjects had not used any alcohol, illicit substance or medication for at least 15 days prior to enrollment. All subjects gave written informed consent, and the study protocol was approved by the Ethical Committee of Gülhane Military Medical Faculty.

Following completion of the semi-structured clinical interview form, the SCID-I and SCID- II were used by a psychiatrist for establishment of diagnosis. Completion of the Buss-Perry Aggression Questionnaire, and the measurement of the ERPs were performed in the second phase of the study.

Scales

A- Semi-structured Clinical Interview form: Socioeconomic characteristics, alcohol and substance use, suicidal thoughts and self-injury were questioned.

B- Aggression Questionnaire: This questionnaire includes 34 items with five sub-scales and has been developed by Buss-Perry to evaluate the anger and aggressiveness (17). These sub-scales evaluate physical aggression, verbal aggression, anger, hostility, and indirect aggression. Since there is no cut-off point, the degree of aggression is determined by the total score (≤29: very low, 30-39: low, 40-44: medium low, 45-55: medium, 56-59: medium high, 60-69: high and ≥70: very high). Sub-scale scores should be taken into consideration if the Aggression Questionnaire total score (AQT) is high. Validity and Reliability of BPAQ has been demonstrated by Can in 2002 (18). The internal consistency was reliable with a Cronbach alpha coefficient of 0.95. The test-retest reliability for the BPAQ was also satisfactory (correlation r= 0.482-0.760, physical aggression r=0.847, verbal aggression r=0.696, anger r=0.746, hostility r=0.810, indirect aggression r=0.857, total aggression r=0.857).

Electrophysiological evaluation

Electrophysiological Method and Measurements: Subjects were tested blindfolded in a quiet room. The test was performed using an ESAOTEBIOMEDICA 4-channel (Italy) EMG-EP device. Bio-electric signals were recorded at Pz, Fz, and Fpz points along the midline by using superficial electrodes (disc shaped with 11mm diameter, DANTEC Electronic A/S, Denmarc) and the international 10-20 EEG electrode placement system. The ground electrode was placed at the mid-line between the Fpz and Fz points. Reference electrodes were placed on the mastoids. To monitor eye movements, one electrode was placed infraorbitally (IO). Impedances were selected as < 5K and the filter range was between 0,5-50 Hz with an analysis time of 1000 ms. The sound intensity was increased until the appropriate counting was detected. Although the sound intensity showed individual variations, generally it was 60dB. Before the test was initiated, the subjects had to be checked for the counting process for one minute. BAEP records were taken during the task including the sound discrimination paradigm. Ear phones were placed over the patient's ears delivering non-target (frequent 3000 Hz) and target (rare 2000 Hz) stimuli with a mean hearing threshold of 60 dB and a pulse duration of 5.3 ms. The stimulus frequency was 0.7 Hz. Subjects were asked to count the target stimuli (2000 Hz). Target and non-target stimuli were delivered randomly at rates of 20% and 80%, respectively. The average value of the 40 target stimuli obtained without artifact was calculated and the test was repeated. This paper presents the analysis of the N2 and P3 potentials obtained from Pz and Fpz. The calculation was performed by taking into account the data from the peak point of N2 to the peak point of P3 for P3; from the peak point of P1 to the peak point of N2 for N2. Calculation of the latencies was performed by considering the midpoint of each potential.

Statistical analysis

Continuous parametric and non-parametric variables were compared between the independent groups by the t test and Mann- Whitney U test, respectively. Groups in compliance with the normal distribution of the values obtained were analyzed by the Kolmogorov-Smirnov test. Categorical data were analyzed with the chi-square test.

Statistical analysis was performed using "SPSS 16.0 for Windows". Significance has been accepted as p<0.05.

RESULTS

There were no significant differences between the two groups with respect to age, education, and marital status (Table 2). There were significant differences between the two groups with respect to suicidal thoughts (z:-7.025, p=0.001), self-injury (z:-7.292, p=0.001), alcohol use (z:-6.377, p=0.001) and regular employment (z:-6.645, p=0.001).

however, the P3 amplitude values were detected to be significantly lower in the ASPD group than in the controls (p<0.01).

DISCUSSION

It has been shown that both groups were selected in accordance with the the study protocol, since there was no difference between the ASPD and the control groups in age, education, marital status and gender (Table 2). There were significant differences between the two groups regarding suicidal tendency, self-injury, alcohol, and regular employment, as expected, because classically, antisocial personality disorder is characterized by anger, violent behavior, impulsivity, alcohol or substance abuse, self mutilation, and unemployment (19).

Table 2: Socio-demographic characteristics of the ASPD and control groups

	Groups	Mean ±SD		P	t (8z)	
Age	Control ASPD	22,8±2,1 23,4±2,6		0,22	-1,2	†
Education	Control ASPD	5 (5-13) 5 (5-13)		0,87	-0.156	††
Marital status		Single ----------	Married ----------	0,15	df ------	†††
	Control	41	3		1	
	ASPD	35	7			

SD: Standard Deviation, N: Subject number, df: degree of freedom, †:in independent groups, t test††: Mann Whitney U test, ††† X2 test

Table 3: Correlations between the BPAQ Total scores and electrophysiological measurements

	R	p
LN2	0,01	0,92
AN2	0,09	0,54
LP3	-0,21	0,17
AP3	-0,12	0,41

LN2: N2 Latency, AN2: N2 Amplitude, LP3: P3 Latency, AP3. P3 Amplitude

There were no correlations between the LN2, LP3, AN2, AP3 values and the BPAQ total scores in either group.

In the ASPD group, the BPAQ Total Score, Physical Aggression, Verbal Aggression, Anger, Hostility and Indirect Aggression values were significantly higher than in the controls (p<0.001).

Although the latencies of the N2 and P3 components were shorter and the amplitude of N2 was lower in the ASPD group compared to the controls, these differences did not reach statistical significance (Table 4, figure 1-2);

Costa et al. (2000) have found a significant correlation between the amplitude of P3, childhood behavior disorders and adult ASPD signs (20). In our study, we did not find any correlation between aggression, the most prominent finding of the ASPD diagnosis, and the ERP components (Table 3).

Results of a study, in which the visual P3 was measured in college students, indicated a significantly reduced P3 amplitude and a prolonged latency for impulsive aggressive subjects (14).

Karaaslan et al. (1999) found that the alcohol-dependent patients had significantly longer LP3. AP3 was not different from that of controls (21). Bond and Surguy (2000) reported that subjects from the normal population with aggressiveness and violence behavior showed a reduced AP3 and a prolonged LP3 (13). Similarly, the AP3 was reduced in our study relative to the control

Table 4: Comparison of the ASPD and control groups for electrophysiological measurements

	Mean ± SD ASPD (N:42)	Control (N:44)	t	p
LN2 (msn)	204.5±20,4	210.9±13,8	01/01/68	0.096†
AN2 (μv)	5.07± 4.06	6.4±4.47	01/01/41	161
LP3 (msn)	312.2±29.32	318.9±3.6	01/01/00	319
AP3 (μv)	10.05±5.88	15.2±7.3	3.6**	<0.001
BPAQ Total Score	68.9±2.8	39.3±6.3	27.7**	<0.001
Physical Aggression	71.36±3.2	42.8±4.5	33.6**	<0.001
Verbal Aggression	66.1±4.74	39.1±6.2	-22.4**	<0.001
Anger	73.1±3.8	46.0±8.8	-18.2**	<0.001
Hostility	66.3±4.9	43.3±6.4	-18.4**	<0.001
Indirect Aggression	64.3±6.6	40.34±5.3	-18.5**	<0.001

LN2: N2 Latency, SD: Standard Deviation, AN2: N2 Amplitude, N: Subject number, LP3: P3 Latency, **:p<0.01, AP3. P3 Amplitude, BPAQ: Buss-Perry Aggression Questionnaire

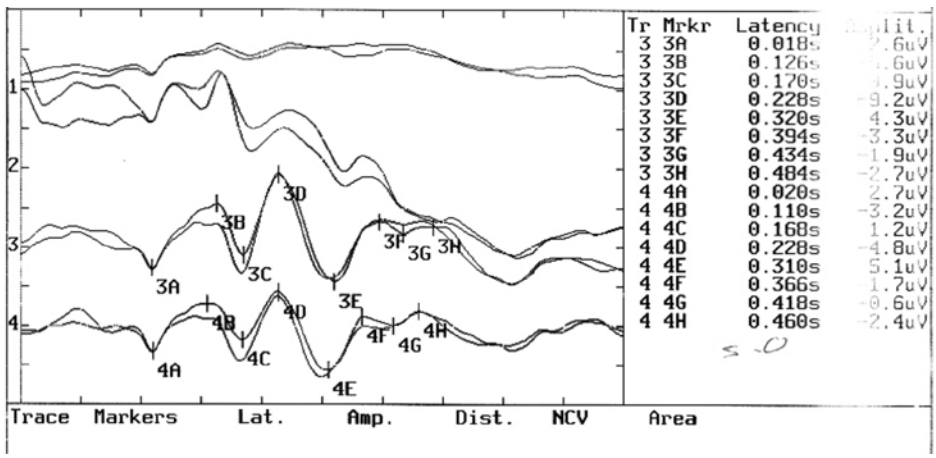

Figure 1: The sample trace obtained from the group with antisocial personality disorder.

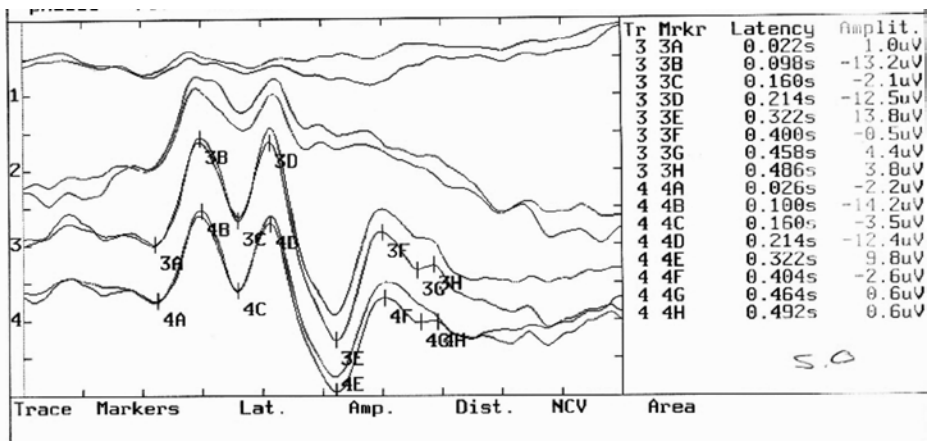

Figure 2: . The sample trace obtained from the control group

group, but LP3 did not show any difference relative to the control group (Table 4). In line with our findings, some authors have suggested that AP3 was reduced, whereas LP3 didn't change in patients with antisocial personality disorder (22).

Subjects from the normal population with aggressiveness and violent behavior showed a reduced AP3 and a prolonged LP3. It has been suggested that a

reduced AP3 could be an indicator for violent behavior and aggressiveness (13).

In their study, Kiehl et al. (2006) demonstrated an increased AN2 and a reduced AP3 in psychopathic subjects (15). In contrast with Kiehl's result, Gillian et al. (2007) detected a reduced AN2 in psychopathic subjects (23). Dong et al.(2009) indicated that the N2 potential was associated with the successful suppression of the behavioral response in the impulse control process (24). In our study, there was no difference in AN2 values between the antisocial group, characterized by impulsive behavior, and the healthy control group (Table 4). This finding may point out that there is no relationship between AN2 and the suppression of the behavioral response in the impulse control process.

Many studies have emphasized the association between aggressive/impulsive behavior and the AP3. Recently, Zukov et al. (2008) have found an association between aggressive/impulsive behavior and reduced AP3. AP3 was reported to be reduced in alcohol dependence, substance and nicotine dependence, behavioral disorders, and antisocial deviance (13,15,23). In line with the literature, we found that AP3 was significantly reduced in the ASPD subjects (Table 4). The high rate of co-morbidity of antisocial personality features and alcohol/ substance dependency may cause methodological complications in some study samples. Additionally, owing to the fact that individuals with antisocial personality disorder display a low frustration tolerance, it is difficult to block or stop alcohol and drug abuse even in the absence of alcohol or substance addiction (26). Our study is noteworthy because the study sample had no confounding factors such as alcohol or substance abuse. On the other hand, the inclusion of only male subjects into the trial represents a limitation.

In conclusion, the reduced AP3 values obtained in the ASPD sample with high aggression scores but without confounding factors such as alcohol or use substance were in line with the literature. In contrast to literature reports, no prolonged LP3 values were detected in the group with high aggression scores (Table 4). The relevant study data from the literature remains controversial. Further studies with larger samples are obviously required. In addition, the social, cultural and ethnic differences in these fields represent other important areas which need to be studied.

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