# Original Article

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# Comparison of Visual Evoked Potential in Patients with Attention-deficit/Hyperactivity Disorder in Medication and Non-medication Group

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**Aim:** Attention-deficit/hyperactivity disorder (AD/HD) is a common neuropsychiatric disorder resulting from disruptions in circuits that regulate attention and action. Many studies have revealed different parameters of AD/HD through neurophysiological measurements. The purpose of this study is to compare visual evoked potentials (VEPs) latency and amplitude in AD/HD patients. This study aims to discuss the effects of disease severity and psychostimulants use on the central nervous system based on VEP measurements.

**Methods:** The study was designed using a retrospective-descriptive methodology, including a total of 30 patients diagnosed with AD/HD, 15 of whom were taking psychostimulant medication and 15 of whom were not, who presented to the psychiatry outpatient clinic between January 2024 and June 2024. P-100 amplitude and latency were recorded for both eyes. In AD/HD patients, these values were compared based on the severity of the disease, between those who receive treatment and those who do not.

**Results:** There was no statistically significant difference between latency and amplitude values according to disease severity. The difference was statistically significant between P-100 latency according to psychostimulant use (p=0.046, p=0.016). With regard to the use of psychostimulants, there was no significant difference in the amplitude values.

**Conclusion:** VEP studies with increased sample size AD/HD, with additional confounding variables, will provide insight into information processing and shed light on the pathophysiology of AD/HD.

**Keywords:** Attention-deficit/hyperactivity disorder, visually evoked potentials, P-100

# Introduction

Attention-deficit/hyperactivity disorder (AD/HD) is a chronic, heritable neurobehavioral condition marked by impulsivity, hyperactivity, and inattention, and affects 1.4-3% of the population (1). Approximately 60% to 80% of AD/HD symptoms last throughout adulthood. Therefore, AD/HD is not exclusively a childhood condition that subsides on its own after adolescence, and 4.4% of adults on average experience it (2). Although there are similarities in adult and childhood symptomatology, there are also important differences. Adults frequently experience emotional dysregulation, inattention compensated

through depressive and anxious mechanisms, executive function (EF) -related symptoms, substance use disorders, and sleep disorders (3). Adults and children with AD/HD have varying levels of impairment in EFs, according to studies. The ability to mentally engage with ideas, wait before acting, meet unique, unexpected problems, resist temptations, and maintain attention is an example of EFs (4). Basic cognitive processes like attention management, cognitive inhibition, inhibitory control, working memory, and cognitive flexibility are examples of EFs, which are a fundamental to cognition (5). Working memory, also known as short-term memory, is affected in AD/HD,

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where cognitive control, self-direction, self-regulation, and stimulus-driven behavioral responses are impaired, and is encoded with visual and auditory stimuli (6).

Researchers have used neurophysiological examinations to elucidate and correlate the complex neural pathways and etiology of neurodevelopmental mental diseases, such as AD/HD. Few studies have investigated visual evoked potential (VEP) patterns as a helpful tool for understanding visual processing (7). VEPs are electrical potentials triggered by brief visual stimuli, and recorded from the scalp the overlying the visual cortex. Signal averaging is used to extract VEP waveforms with an electroencephalogram (EEG) (8). Electrical changes in the central nervous system (CNS) caused by external stimuli are frequently recorded using evoked potentials. Clinically, short-latency brainstem auditory evoked response, somatosensory evoked potential, and VEPs are used. These evoked potentials represent the neuronal response to the given stimulus. Their amplitudes and latency are determined by the stimulus's physical properties. These waves have been researched in a variety of neurological and psychiatric syndromes, particularly schizophrenia, some types of anxiety disorders, and epilepsy. It is a noninvasive procedure that provides information about neural activity connected to sensory and cognitive information processing (9).

The goal of this study was to compare VEP latency and amplitude in one treated and one untreated group of 30 AD/HD patients, 15 of whom are on psychostimulant medication, and 15 of whom are not. We hypothesize that the cognitive impacts of disease severity and medication use in individuals with AD/HD can be demonstrated by VEP measurements.

# **Materials and Methods**

Written informed consent was obtained from the patients in line with the ethical rules stated by the Declaration of Helsinki. Ethics approval was received on 09.03.2023 with approval number 2023-21, from the Scientific Research Ethics Committee of University of Health Sciences Türkiye, Kocaeli Derince Training and Research Hospital where the study was carried out.

#### **Patients and Data**

The sample size was calculated with power analysis by G\*Power version 3.1.9.4. The minimum sample size was determined as 22 patients, with 11 patients in each group, based on the reference study and normal standard deviation at a 95% confidence level (1.81), as cited in the reference study (2).

Thirty patients aged between 18 and 65 years who applied to University of Health Sciences Türkiye, Kocaeli Derince Training and Research Hospital Psychiatry

Outpatient Clinic with a diagnosis of AD/HD were included in the study. From this patient group, 15 patients who used psychostimulant drugs, and 15 who did not use them, were admitted to the psychiatry outpatient clinic between January 2024 and June 2024. The adult AD/HD Diagnostic Screening and Rating Scale, which has been validated for Turkish populations, was applied to all participants (10). The scale is a five-point Likert-type rating scale and consists of three subsections: Section 1, Attention Deficit: This section contains nine items based on symptoms of AD according to Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). Section 2: Hyperactivity/ Impulsivity Section: This section also contains nine items based on symptoms of hyperactivity according to DSM-IV. Section 3: Characteristics and Problems Related to ADHD (Problem): This section, based on clinical experience and observations, contains a total of 30 items. The patients with total scores below 20 were considered mild, between 20-59 moderate, and above 59 severe AD/HD. Visual evoked potential measurements were performed on all patients. The obtained VEP measurements were compared according to the patients' disease severity and treatment status.

Participants had no eye disease, anisocoria, or pupillary abnormality. Visual acuity was normal, and no myotic or mydriatic drops were used.

#### **Study Design**

Pattern visual evoked potential were recorded with a Viasys Medelec Synergy device. Pattern visual evoked potential tests were performed in a dark, sound-isolated room. Surface electrodes were used, ensuring that the scalp was cleaned and the electrodes were entirely placed. The active electrode was placed 2 centimeters above the external occipital protuberance; the reference electrode was placed on the vertex; and the ground electrode was placed on the scalp border on the forehead.

The recordings were made in a 1-degree pattern size according to the International Society for Clinical Electrophysiology of Vision protocol. While the patients were looking at the fixation point the middle of the moving chessboard pattern on the screen 1 meter in front of them, the electrical potentials at the occipital cortex were recorded. The black-white chessboard pattern reversed at 2 reversals per second.

An average of 100 waves was recorded. The latency was measured in milliseconds (ms) and the amplitude was measured in microvolts (mV). The contrast was measured to be 99% according to the Michelson constant. When the cover or environmental artifacts exceeded 5%, the study was repeated.

Two negative waveforms (N75 and N135 peaks) and one positive waveform (P-100 peak) were recorded

for each eye (Figure 1). All recordings were made with every participant's eyes closed. Participants were closely followed by an experienced electrophysiology technician who ensured that they looked at the fixation point. Records were repeated for both eyes, of all patients, to ensure accuracy. P-100 latency and amplitude for both eyes of all patients were compared.

## **Statistical Analysis**

Statistical Package for Social Science (IBM SPSS Statistics 25 software, Armonk, NY: IBM Corp.) was used for data analysis. Descriptive statistical methods were used. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as numbers. Metric data with a normal distribution were compared using the independent samples t-test. The Mann-Whitney U test was used to analyze the presence of significant differences when data were non-normally distributed. A p-value under 0.05 was considered statistically significant.

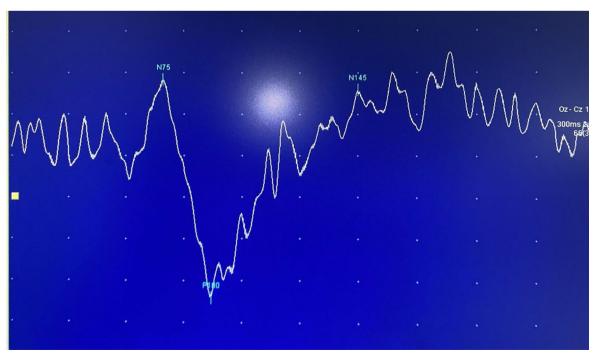
## **Results**

Thirty patients were included in the study; 19 were male and 11 were female. Five women and 10 men were using psychostimulant drugs. The mean age of all participants was 25.53±8.1, while the mean age of women was 24.91±7.1 and that of men was 25.89±8.9. There was no statistically significant difference in the age or the gender distribution of the patients.

Adult AD/HD Diagnostic Screening and Rating Scale was applied to all patients. Eight (26.7%) of the patients were moderate and the other 22 (73.3%) were diagnosed with severe AD/HD. Five (62.5%) of the patients with moderate AD/HD were on medication, while 10 (45.5%) of the patients with severe AD/HD were on medication (Table 1).

The pattern VEP right P-100 latency, right P-100 amplitude, left P-100 latency, left P-100 amplitude, and mean P-100 latency values of all patients were compared. Mean left P-100 latency was 103.86±5.0 ms. Right P-100 latency was 105.73±5.6 ms. Left P-100 amplitude was 11.1±4.0 mV. Right P-100 amplitude was 10.6±4.4 mV. Four VEP values of each patient were compared according to medication use and AD/HD severity (Table 2).

The mean right P-100 latency of AD/HD patients who were taking medication was 107.6±4.7 ms, and of those who were not taking medication was 101.1±4.8 ms. The left P-100 latency of AD/HD patients who were taking medication was 108.4±4.8 ms, and of those who were not taking medication was 103.0±5.2 ms. The difference was statistically significant between P-100 latency according to pshycostimulant use (p=0.046, p=0.016). When the mean of right and left P-100 latency values were compared in the two groups, the difference was also statistically significant (p=0.008).



**Figure 1.** VEP-N75, P100, N145 waves *VEP: Visual evoked potential* 

Table 1. Demographics and clinical characteristics of the groups								
Characteristics	Medication (n=15)	Non-medication (n=15)	Total (n=30)	p-value				
Age (years), mean ± SD	25.89±8.9	24.91±7.1	25.53±8.1	0.72				
Gender (M/F)	10/5	9/6	19/11	0.71				
AD/HD score, mean ± SD	58.4±10.2	56.7±9.8	57.6±9.9	0.65				

Data are presented as mean  $\pm$  SD or n. An independent samples t-test was used for normally distributed continuous variables. The Mann-Whitney U test was used for non-parametric data. P<0.05 was considered statistically significant

AD/HD: Attention-deficit/hyperactivity disorder, SD: Standard deviation, M: Male, F: Female

Table 2. P-100 values according to psychostimulant use and adhd severity									
	Psychostimulant medication		n value	AD/HD severity		n value			
	Under-medication	Non-medication	p-value	Moderate	Severe	p-value			
Left P-100 latency (ms)	108.4±4.8	103.0±5.2	0.046*	106.4±5.2	103±4.7	0.098			
Right P-100 latency (ms)	107.6±4.7	101.1±4.8	0.016*	105.8±4.4	105.6±6.1	0.777			
Mean P-100 latency (ms)	107±3.9	102.6±4.6	0.008*	106.1±4.4	104.3±4.9	0.368			
Left P-100 amplitude (mV)	10.4±3.9	11.9±4.2	0.321	9.4±2.6	11.8±4.4	0.163			
Right P-100 amplitude (mV)	10.6±4.7	10.7±4.3	0.974	8.7±2.8	11.4±4.7	0.150			
Mean P-100 amplitude (mV)	10.5±4.2	11.3±4.1	0.614	9.1±2.6	11.6±4.4	0.143			

Data are presented as mean ± SD or n. Independent samples t-test was used for normally distributed continuous variables. Mann-Whitney U test was used for non-parametric data. A p-value <0.05 was considered statistically significant

P-100 values according to psychostimulant use and AD/HD severity

AD/HD: Attention-deficit/hyperactivity disorder, ms: Millisecond, mV: Microvolt

## Discussion

In our study, left P-100 latency and right P-100 Latency values differed significantly between groups that used psychostimulants and those that did not. There was no noticeable difference when the latency values were compared according to the severity of AD/HD. Attentiondeficit/hyperactivity disorder is a disorder that affects both simple and complicated cognitive processing, even though it involves behavioural problems. Distractibility, slow processing speed, and rising response time variability are examples of basic cognitive processes (11,12). Distractibility is the characteristic that leads individuals to become distracted from the intended stimuli. The failure to store the appropriate stimulus in memory or recording incorrect components is caused by distraction or task diversion. Distractibility in AD/HD is caused by an inability to reject unnecessary data or an excessive amount of attention to task-irrelevant stimuli (13-15). It is still unclear which stage of information processing is affected by attention problems in AD/HD and which regions of the CNS play a role in this problem. According to some theories, the CNS's three neural networks play a significant role in how effectively sustained attention processes are carried out. The alerting network ensures that this state of alertness is maintained and that the reaction is prepared. The excitatory network includes the right parietal lobe, the locus coeruleus and the right frontal lobe, particularly in some higher regions of the 6th Brodmann area. It seems

that noradrenaline has a special role in the excitatory network's operation (16,17). Sensory stimuli are oriented via the orientation network. This network has been the subject of research, particularly with regard to visual stimuli. The parietal lobes, the oculomotor system, and the visual regions, particularly the fusiform gyrus, makeup the majority of the extrinsic network for processing visual stimuli. Acetylcholine appears to play a key role in the functioning of the orientation network (16,18). The executive-control network is focused on regulating intentional behavior, target identification, error detection, problem solving, and restraining automatic responses. This network consists of the basal ganglia and anterior cingulate gyrus. The executive-controller network appears to be particularly dependent on dopamine for proper function (16,19). Adults with AD/HD show impairments in both basic cognitive abilities such as slower processing speeds and increased distractibility and more advanced abilities such as problems with cognitive flexibility, selective attention, planning, verbal fluency, working memory, and memory functions (10,20). From the perspectives of neuroanatomy and chemistry, AD/HD is viewed as a very heterogeneous condition.

Measurement of evoked potentials has been used in several studies in an attempt to explain this complex relationship. Visual evoked potentials are recordings of electrical brain responses that occur in the occipital cortex in response to visual stimuli received by photoreceptors in response to visual stimuli. It measures the duration for

neuronal activity to transit from the retina to the occipital cortex and is used clinically to assess the pathway's integrity and function. The multiple stimulus-dependent waveforms are averaged by standard VEP. However, the positive wave on the midline occipital EEG electrode, marked P-100, which typically occurs about 100 ms after stimulation, is thought to be significant. For many disorders, their amplitude and latency are revealing (21,22). However, research has been conducted to determine whether measuring VEP-based wave qualities can be used to differentiate between various neurodevelopmental, neurodegenerative and mental diseases (23-25). Results from a study comparing VEP values of 12 healthy individuals, 12 patients with AD/ HD, and 12 patients with bipolar mood disorder show that there is a significant difference in the neural activity of the visual systems in response to periodic optical stimuli among individuals with AD/HD, bipolar mood disorder, and healthy controls (2).

In a systematic review of EEG findings in adult AD/ HD, Adamou et al. (26) revealed that EEG measurements differed for this disorder. Reasearch into the relationship between elevated theta (4-8 Hz) levels, alpha waves (8-10 Hz), beta waves (12-25 Hz), delta activity, and gamma band activity in EEG measurements and AD/ HD has revealed inconsistent findings. Low gamma band activity has been observed in adults with AD/HD, which is consistent with research conducted in children and adolescents. The dysregulation of brain networks related to attention function was assumed to be the explanation of this (27-30). Studies focusing on eventrelated potential (ERP) measurements in AD/HD, on the other hand, have discovered these changes can be used as an informative tool. Event-related potentials studies are very beneficial in investigating a specific neural response triggered by cognition. A reaction to cognitive processing, such as viewing stimuli during assessment with scales, causes ERPs, which is a brief segment of the ongoing EEG recording (26,31). In adult AD/HD, it is visible that there is increased variability for both auditory and visual stimuli, as well as slowed cortical activity, which is consistent with the commonly predicted research findings (27,32). According to a study conducted by Leroy et al. (33), findings support the idea that earlier cortical levels of visual processing are impaired in the disorder, resulting in the formation of various ERP generators and EEG patterns in adult AD/ HD. Hasler et al. (34) found that the functional networks responsible for bottom-up and top-down attention were less active, which suggests that people with AD/HD have less cortical capacity for activities involving these processes. There have been few studies that have investigated the severity of AD/HD symptoms, psychostimulant use, and

ERP characteristics. Transcranial Magnetic Stimulation evoked potentials and ERPs were analyzed in a study by Hadas et al. (35); and right prefrontal cortex excitability was closely linked with AD/HD severity and behavioral impulsivity. According to studies assessing the severity of symptoms using ERP components such as mismatch negativity, it appears to predict the severity of AD/HD symptoms in children and adolescents. These results support the use of ERPs in assessing AD/HD symptoms in patients (36,37).

Methylphenidate (MPH) is the most commonly prescribed AD/HD medication as it helps increase and maintain alertness, tackle fatigue, and enhance focus. improvements in cognition, such as working and episodic memory (38,39). By comparing the ERPs of participants with AD/HD, following treatment with MPH, to participants who received a placebo, some EEG research in this field has attempted to answer this question. Unfortunately, findings for the N1, N2, P2, and P3 components' amplitudes and latencies varied between analyses (40,41).

## **Study Limitations**

Including a larger number of volunteers in the study is important for the consistency of the results. In this respect, it is important that future studies in this field be conducted with a larger number of patients. Additionally, no comparison was made in the study regarding the medication types, doses, and the periods of intake by the patients due to difficulty in classification. Another limitation of the study is the lack of healthy control group and the exclusion of EEG findings. The strength of the study is that it is the first study to examine confounding factors that may affect information processing speed, such as disease severity and treatment intake, using neurophysiological measures of visual processing speed.

#### Conclusion

This study shows that the P-100 latency, which indicates the optic nerve to occipital cortex conduction, is longer in AD/HD patients using psychostimulant medication. This would suggest an additional process in the conditioning phase of a stimulus rather than the recording phase. As expected, if the distractibility and disease severity caused a difference between the treated/untreated and moderate to severe groups, longer latencies and smaller amplitudes would be expected in untreated and severe patients. Larger sample size VEP studies in AD/HD with additional confounding factors will provide an understanding of information processing and elucidate the pathophysiology of this disorder.

#### **Ethics**

**Ethics Committee Approval:** Ethics approval was received on 09.03.2023 with approval number 2023-21, from the Scientific Research Ethics Committee of University of Health Sciences Türkiye, Kocaeli Derince Training and Research Hospital which the study was carried out.

**Informed Consent:** Written informed consent was obtained from the patients in line with the ethical rules stated by the Declaration of Helsinki.

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#### **Footnotes**

## **Authorship Contributions**

Concept: B.K., Design: Z.U., Data Collection or Processing: B.K., Z.U., Analysis or Interpretation: B.K., Z.U., Literature Search: B.K., Z.U., Writing: B.K., Z.U.

**Conflict of interests:** No conflict of interest were declared by the authors.

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