

Electroencephalographic Findings in Children with Attention Deficit Hyperactivity Disorder

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Abstract

Objective: The relationship between cognitive functions, EEG findings and epilepsy in patients with ADHD is controversial. The aim of this study is to determine the frequency of EEG abnormality and its relationship with clinical findings of children with ADHD.

Methods: A total of 434 children's sleep and/or awake EEG who received the diagnosis of ADHD were taken regardless of seizure history.

Results: A total of 21.9% epileptic and 15.2% nonepileptic discharges were detected in EEG. Epileptic discharges were found to be more common in the attention deficit type of ADHD, in right hemisphere regions and were significantly higher in patients who had sleep EEG compared to those who had awake EEG ($p < 0.0001$).

Conclusion: The presence of EEG abnormalities in patients with ADHD is associated with clinical findings. Interictal epileptic discharges could affect cognitive functions. EEG recordings including sleep should be taken even in the absence of seizure history.

Keywords: Attention deficit hyperactivity disorder; Electroencephalography; Epilepsy; WISC-R scores; Cognitive functions

Introduction

Attention deficit hyperactivity disorder (ADHD) which is one of the most common disorders seen in child psychiatry clinics and manifests with impulsivity not suitable for the child's developmental level of age, short attention time and hyperactivity [1].

Studies reported that ADHD is frequently coexist with epilepsy in childhood [2]. The incidence of epilepsy and rate of electroencephalography abnormalities in children with attention-deficit hyperactivity disorder appears to be more expected than the normal population from the result of studies [3,4]. A meta-analysis of electroencephalography (EEG) findings in children with ADHD showed that theta waves were more frequent in the ADHD group while beta waves were more frequent in healthy controls. The theta/beta ratio was found to be higher in frontal and central regions in approximately 90% of patients with ADHD and only 10% of primary beta activity in the same regions, respectively. These results show the reduction in cortical arousal and are thought to result in a delay in maturation in attention regulating systems [5]. The presence of epileptic activity in EEG in the children with ADHD have been reported at different rates, such as 6.1-26% [6,7].

The aim of this study was to examine the findings of the EEG in patients with ADHD with or without a history of seizure; determine the rate of epilepsy and EEG abnormalities in these patients; determine

whether markers for the groups who have a risk for epilepsy, evaluate the association between the presence of EEG abnormalities and clinical findings and to provide a new clinical follow up in the light of these data.

Methods

This prospective study was composed of 434 patients between the ages of 3-17 years who received a diagnosis of attention deficit and hyperactivity disorder at the İnönü University Department of Child Neurology and Department of Child and Adolescent Psychiatry outpatient clinics within 2 years. İnönü University child neurology department is a reference center in Eastern Anatolia that about 15,000 patients seen each year. The patients' gender, age, symptoms associated with ADHD, seizure and family history of similar illness and neurological-systemic disease were recorded. Sleep and/or awake EEG were taken from all patients as once with recording time 20 minutes regardless of the presence of history of seizures. Scalp EEG electrodes were placed according to the International 10-20 system. Recordings were made with 21-channel EEG Grass-Telefactor A540 model and evaluated by an instructor of child neurology. Irregularity of baseline activity and focal or asymmetric slow wave activity on EEG were termed as nonepileptic discharges.

The diagnosis of ADHD was evaluated according to DSM-IV-TR diagnostic criteria [1]. The Atilla Turgay DSM-IV-Based Child and Adolescent Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S) was used for determining the subtypes of ADHD [8-11]. This scale was developed by Turgay and measures disruptive behavioral problems based on DSM-IV diagnostic criteria [11]. It was adapted to

Turkish by Ercan [12,13]. T-DSM-IV-S is also a four-point Likert-type scale. Nine items in this scale assess severe hyperactivity-impulsivity, 9 items assess attention-deficit, 8 items assess oppositional behavior and 15 items assess symptoms of conduct disorder. The WISC-R evaluation showing intelligence level was performed in patients >6 years and patients were evaluated as being borderline intellectual functioning if their level was 71-84, mild mental retardation if at 50-55 to approximately 70, moderate mental retardation if at 35-49 to 50-55, severe mental retardation if the level was 20-25 to 35-40 and profound mental retardation if at 20-25.

The statistical package SPSS for Windows version 16.0 was used for statistical analysis of the data. Measurable variables were expressed as mean±standard deviation and categorical variables as a number and percentage. The result of the evaluation of the measurable variables with the Shapiro Wilk normality test did not show a normal distribution between the groups (p<0.05). For this reason, an independent sample t test was used to compare the patient and control groups. Fisher's exact chi-square test and Pearson's chi-square test was used for comparison of the groups in categorical (qualitative) variables. p<0.05 was considered statistically significant. Associations between categorical variables were assessed using multivariate regression analysis.

Results

A total of 434 patients with a diagnosis of ADHD composed of 127 girls (29.3%) and 307 males (70.7%) were included in this study. The male/female ratio was 2.4/1 respectively. The mean age of patients was 8.9 ± 3.16 years (3-17).

An EEG was obtained from 69.4% of the patients after sleep deprivation and 30.6% of the patients while awake from a total 434 patients. EEG findings were found to be normal in 62.9% (273/434) of the cases and abnormal in 37.1% (161/434). A total of 21.9% of the patients (95/434) have epileptic abnormalities and 15.2% (66/434) have nonepileptic discharges from 161 patients with abnormal EEG findings. Epileptic EEG abnormalities were detected as focal in 14.5% (63/434) of cases and generalized in 7.4% (32/434). Comparison of occurrence-type of seizure and EEG findings between ADHD patients/sleep-awake EEG are shown in Table 1. Epileptic and nonepileptic discharges observed in the right hemisphere accounted for 11.8% (51/434) of patients while in the left hemisphere were 8.5% (37/434) of patients. Focal findings seen in the frontotemporal region in 3% (13/434) of patients, in the frontocentral region in 2.8% (12/434) of patients, in the temporoparietooccipital region in 2.3% (10/434) of patients, in the temporal region in 2.3% (10/434) of patients and in other areas 89.6% (35/434) of patients. A total of 20.5% of patients (89/434) have clinical seizure history. Seizures were generalized in 18.7% (81/434) of patients and partial in 1.8% (8/434) of patients. Treatment was given to 26.5% (115/434) of patients with clinical seizures and abnormal EEG findings. A total of 23.3% (101/434) of patients have received monotherapy and 3.2% (14/434) polytherapy. Clinical history of seizures and generalized seizures were significantly higher in patients who had sleep EEG over those with awake EEG (p<0.0001, p<0.0001). EEG abnormalities and epileptic EEG findings were more frequent in patients who had sleep EEG (p<0.0001, p<0.0001). Results are provided in Table 1. Focal EEG abnormalities were found to be more frequent in the right hemisphere in patients who had sleep EEG over those with awake EEG (p=0.036). The frequency of epileptic seizures was found to be significantly higher in

patients who had epileptic EEG abnormalities compared to those who had normal findings and nonepileptic discharges (p<0.0001).

	Sleep EEG	Awake EEG	Total	p
	(n=301)	(n=133)	(n=434)	
Seizure	80 (%26.6)	9 (%6.8)	89 (%20.5)	<0.0001
Type of seizure				
Generalized	75 (24.9)	6 (%4.5)	81 (%18.7)	<0.0001
Focal	5 (%1.7)	3 (%2.3)	8 (%1.8)	
EEG findings				
Normal	166 (%55.2)	107 (%80.5)	273 (%62.9)	
Nonepileptic	47 (%15.6)	19 (%14.2)	66 (%15.2)	<0.0001
Epileptic	88 (%29.2)	7 (%5.3)	95 (%21.9)	
Generalized	30 (%10)	2 (%1.5)	32 (%7.4)	
Focal	58 (%19.2)	5 (%3.8)	63 (%14.5)	

Table 1: Comparison of occurrence-type of seizure and EEG findings between ADHD patients/sleep-awake EEG.

From a total of 240 patients who have determined subtypes of ADHD, 115 patients (48%) were found to have a combined type, 39.5% (95/240) were inattentive type and 12.5% (30/240) had the hyperactive type. Seizure, seizure type and EEG findings were compared between subtypes of ADHD and there was no statistically significant difference between the groups. But EEG abnormality and epileptic discharges were found most common in the inattentive than the combined type and hyperactive type. Comparison of occurrence-type of seizure and EEG findings between ADHD subtypes are summarized in Table 2.

	ADHD-C*	ADHD-H*	ADHD-I*	p
	(n=115)	(n=30)	(n=95)	
Seizure	23 (%20)	3 (%10)	24 (%25.3)	0.336
Type of seizure				
Generalized	21 (18.3)	3 (%10)	21 (%22.1)	0.669
Focal	2 (%1.7)	0	3 (%3.2)	
EEG findings				
Normal	72 (%62.6)	23 (%76.6)	54 (%56.8)	0.196
Nonepileptic	18 (%15.6)	2 (%6.7)	20 (%21)	0.382
Epileptic	25 (%21.8)	5 (%16.7)	21 (%22.2)	0.906
Generalized	9 (%7.8)	3 (%10)	7 (%7.4)	
Focal	16 (%13.9)	2 (%6.7)	14 (%14.7)	

*ADHD-I=Inattentive type, ADHD-H=Hyperactive type, ADHD-C=Combined type

Table 2: Comparison of occurrence-type of seizure and EEG findings between ADHD subtypes.

Average verbal WISC-R values were detected to be 79.6 ± 18.89 (36-116), the average performance values were 85 ± 19.82 (29-133) and the average total values were 81.1 ± 18.66 (43-126) in 190 patients who had a reviewed WISC-R test at the first application before treatment. The results of WISC-R values were compared with clinical seizures and EEG findings in patients and no statistically significant difference were found in terms of verbal, performance and total values. However verbal, performance and total values of WISC-R were significantly lower in patients who had EEG abnormalities ($p = 0.0001$). The patients were divided into 3 groups, mental retardation (<70), dull intelligence (70-84) and normal intelligence (≥ 84) according to the WISC-R total values and were compared with the presence of seizure

and EEG findings. Clinical seizures were more frequent in patients who have a total value of WISC-R<70 although it was not statistically significant. The patients who have EEG abnormalities and in those with epileptic EEG, have lower mean WISC-R values than the patients who have normal EEG ($p=0.001$ and $p=0.008$, respectively). Results are provided in Table 3. The risk of epileptic discharge have found 2.9 times more likely (OR:2.9, 95% CI (1.2-7.2)) and focal epileptic discharges have found 5.4 times more likely (OR:5.4 95% CI (1.12-26.5)) in EEG in patients who have a total value of WISC-R<84. Clinical history of seizures was identified as a risk factor for neuropsychological outcome in patients who have a total value of WISC-R<84 (OR:0.5 95% (0.24-1.02).

	Wisc-R scores (mean \pm SD)			p	Wisc-R scores (mean \pm SD)			p
	Verbal	Performance	Total		<70 (n=89)	70-84 (n=37)	≥ 84 (n=65)	
Seizure								
Yes	78.8 \pm 20.07	75.2 \pm 18.08	74.9 \pm 18.38	0.574	24(%27)	8(%21.6)	8(%12.3)	0.087
No	80.7 \pm 18.99	86.75 \pm 19.4	82.8 \pm 18.44		65(%73)	29(%78.4)	57(%87.7)	
EEG findings								
Normal	83.5 \pm 17.98	89.1 \pm 19.51	85.7 \pm 17.49		47(%52.8)	26(%70.3)	53(%81.5)	0.001
Epileptic	71.5 \pm 18.54	77.2 \pm 18.50	71.4 \pm 18.40	<0.0001	26(%29.2)	7(%18.9)	8(%12.3)	0.008
Nonepileptic	73.4 \pm 18.76	77.7 \pm 18.09	74.1 \pm 17.08		16(%18)	5(%13.5)	4(%6.2)	

Table 3: Comparison of Wisc-R scores in occurrence of seizure and EEG findings.

Discussion

ADHD is covered under the title "attention deficit and disruptive behavior disorders" in the DSM-IV [3]. The disorder has been defined by three sub-types and 18 symptoms in the DSM-IV and is required to have at least six symptoms from either of two nine item lists for the diagnosis [9]. It is emphasized that signs and symptoms should continue for at least 6 months. Three subtypes of ADHD are identified according to attention deficit and hyperactivity/impulsivity dimensions: 1. Inattentive type [ADHD-I] 2. Hyperactive type [ADHD-H] 3. Combined type [ADHD-C] [10].

The prevalence of ADHD in children and adolescents is estimated to be 3-5% in DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV) and 5% in the world according to the global ADHD working group data [2]. The prevalence of ADHD in our country has been reported to be 5-8.1% [8]. Male/female ratio has been reported as ranging from 3-5/1 to 9/1 in clinical trials, while 2/1 in community studies [14]. Social-sample studies conducted in Turkey showed male/female ratios to be 1.8/1 and 2.75/1 [8]. In this study, the male/female ratio was 2.4/1 similar to the studies in the literature and our country, respectively.

There have been many studies on the EEG, one of the etiological views of ADHD. Hughes et al. [15] found 68.8% of some type of spike activity and 30.1% epileptic activity in one study of 176 ADHD patients. Focal discharges were seen in 23.9% of the cases and were more commonly on the left side with the vast majority of occipital and temporal regions. In our study, epileptic abnormalities were detected in

21.9% of the cases and nonepileptic discharges in 15.2% of patients. Focal discharges were detected in 14.5% of the cases, in the right frontotemporal and frontocentral regions. SPECT, PET [13] and fMRI [16] studies in ADHD cases showed statistically significant hypoperfusion, low glucose metabolism and hypoactivity, especially in the right hemisphere and prefrontal-frontal regions.

Hemmer et al. [17] studied 234 cases of ADHD and detected 15.4% epileptic activity, 61% focal abnormalities in EEG. Seizure history was found in 10% of patients with epileptic EEG abnormalities and in 0.6% of patients with normal/nonepileptic EEG abnormalities. In our study, seizure history was detected in a total of 20.5% of the cases, in 63% of patients with epileptic EEG abnormalities and in 6.2% of those with normal EEG. The high proportion of epileptic seizure history determined in cases with epileptic EEG abnormalities was found to be important in determining the risk of epilepsy in patients with ADHD. The risk for having seizures was significantly higher in ADHD patients with epileptic EEG abnormalities [18]. Therefore, patients should be closely monitored in the follow-up stage and initiation of antiepileptic therapy should be considered especially if there are underlying risk factors and having seizures.

Rolandic spikes on EEG have been identified in 5.6% of 483 patients with ADHD in one study [19]. The ratio was found to be higher in the combined type than the inattentive type. Epileptic EEG findings in our study were found most common in the inattentive (22.1%), than the combined type (21.7%) and hyperactive type (16.7%). Epileptiform activity may cause functional changes itself although there is no organic brain lesion [19]. The combined subtype should be assessed

especially in terms of clinical seizures and interictal epileptic discharges on EEG. Clarke et al. [20] examined EEG findings according to subtypes of ADHD cases and determined a high rate of theta activity and lower rate alpha activity in the combined type than the inattentive type. Theta/alpha and theta/beta ratios were found to be different among the groups. A high rate of theta activity determined in ADHD subjects in the literature is thought to be a deviation of development [20]. Absolute alpha and beta with relative delta ratios are changes reflecting maturation with age.

Awake EEG were evaluated in the vast majority of studies on ADHD and EEG. Silvestri et al. [21] evaluated the polysomnography video and identified interictal epileptic discharges in 53.1% of 42 cases of ADHD. They found that a large portion of these findings are in the centrotemporal and frontal area. It has been reported that 7.6% of patients have nocturnal seizures. It is an interesting finding that families did not disclose the seizures before the study in these patients. The finding of significantly higher epileptic EEG findings in the group with sleep EEG in our study reflects the importance of the sleep deprivation EEG especially in patients with ADHD without a history of seizures.

Some studies on the WISC-R profiles of children with ADHD indicate that there is a relationship between the WISC-R rating and ADHD, while some studies indicates no or very little correlation [22]. Performance IQ has been found to be 100 ± 15 , verbal IQ 94 ± 13 and total IQ 96 ± 13 within the normal range in the study of Kawatani et al. [23]. Tripp et al. [24] compared verbal, performance and total intelligence quotient of children with ADHD to normal subjects and showed significantly lower coefficients. In our study, patients with seizures were found to have lower WISC-R total values than those without seizures but there was no significant statistical difference. Patients with epileptic EEG findings also have lower rates of the WISC-R values than those with normal EEG ($p < 0.0001$). This situation suggests that the interictal epileptic discharges could affect cognitive functions. But further studies are warranted to determine if interictal epileptic discharges would affect cognitive functions.

Conclusion

In the literature, routine EEG is not often recommended for cases of ADHD but interictal epileptic discharges can lead to temporary cognitive impairment even if there is no seizure history. Landau-Kleffner syndrome and ESES (electrical status epilepticus during early sleep) are the best examples for showing the relationship between severe epileptiform discharges and specific cognitive disorders [21]. According to the results obtained in this study; patients with mental retardation, inattentive and combined subtype of ADHD should be monitored closely for follow-up, further questioned in terms of seizures and should be given at least once sleep EEG even if there is no history of seizures. Higher epileptic EEG findings found in the group who had been given sleep EEG shows the importance of the sleep deprivation EEG.

Limitations of the study

A number of the ADHD patients studied in this paper have also intellectual disability (ID). A large percentage of patients with ID have epilepsy and EEG abnormalities, so this represents a problem in considering the precise relationship between attention disorder and electroclinical abnormalities. It is reasonable that patients with ADHD

and ID have a higher prevalence of EEG abnormalities and epilepsy than those with "pure" ADHD.

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