

Methylphenidate treatment outcomes and gender differences in attentional deficit and hyperactivity disorder with epilepsy: a follow-up study*

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ABSTRACT

Objective: The aim of this study is to investigate the methylphenidate (MPH) treatment response in children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD) with and without epilepsy. **Methods:** Ninety-four children and adolescents with ADHD consisting of 47 with and 47 without epilepsy were enrolled into the study. The patients were evaluated by DSM-IV-TR, the Stroop test, the Conners' Parent and Teacher Rating Scales. The groups were matched with regard to age, gender, ADHD subtype and comorbidity. The Stroop test was performed three times: during baseline (S-1); at the third month of the MPH treatment (S-2); after drug holiday of the treatment with MPH which lasted for six months (S-3). Stroop total time (ST) and Stroop total error+correction (SEC) scores were analyzed. **Results:** The mean ST-3 and SEC-3 scores were significantly higher in cases with ADHD-attention deficit (ADHD-AD) subtype with the epilepsy group compared to ADHD-combined type (ADHD-CT) in the epilepsy group, whereas there was no significant difference detected in the non-epilepsy groups. While in the boys with/without epilepsy and the girls without epilepsy and were demonstrated significant reductions in all recorded ST and SEC scores during/after treatment in comparison with the initial scores, a similar relationship could not be shown for the girls with epilepsy. **Conclusion:** It is noted that gender and the ADHD subtypes may affect drug choice in patient with ADHD cases comorbid with epilepsy. One of the noticeable results of our study is was that the Stroop scores is no significant change with methylphenidate treatment in especially in girls with ADHD and epilepsy. (Anatolian Journal of Psychiatry 2019; 20(6):642-650)

Keywords: epilepsy, attention deficit and hyperactivity disorder, gender, methylphenidate

Epilepsinin eşlik ettiği dikkat eksikliği hiperaktivite bozukluğunda metilfenidat tedavi yanıtı ve cinsiyet farklılıkları: İzleme çalışması

ÖZ

Amaç: Bu çalışmanın amacı, epilepsisi olan ve olmayan dikkat eksikliği hiperaktivite bozukluğu (DEHB) çocuk ve ergenlerde metilfenidat (MPH) tedavi yanıtının araştırmaktır. **Yöntem:** Çalışmaya, 47 epilepsili ve 47 epilepsisi olmayan DEHB'li 94 çocuk ve ergen alındı. Hastalar, DSM-IV-TR, Stroop testi, Conners Ebeveyn ve Öğretmen Değerlendirme Ölçeği ile değerlendirildi. Gruplar yaş, cinsiyet, DEHB alt tipi ve eş tanımlar bakımından eşlendi. Stroop testi üç kez uygulandı: Başlangıçta (S-1), MPH tedavisinin üçüncü ayında (S-2), altı ay süren MPH ile tedavinin ilaç tatilinden sonra (S-3). Stroop toplam süre (SS) ve stroop toplam hata+düzeltilme (SHD) puanları analiz edildi.

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Bulgular: Ortalama SS-3 ve SHD-3 puanları, epilepsisi olan DEHB-dikkat eksikliği (DEHB-DE) alt tipinde epilepsisi olan DEHB-birleşik tipine (DEHB-BT) göre anlamlı derecede daha yüksekti, fakat epilepsisi olmayanlarda DEHB alt tipleri arasında anlamlı farklılık gözlenmedi. Epilepsisi olan/olmayan erkeklerin ve epilepsisi olmayan kızlarda, başlangıç puanlarına göre tedavi sırasında/sonrasında kaydedilen tüm SS ve SHD puanlarında anlamlı düzeyde azalma gözlenirken, epilepsili kızlar için benzer bir ilişki gösterilememiştir. **Sonuç:** Cinsiyet ve DEHB alt tiplerinin, epilepsi ile birlikte olan DEHB olan hastalarda ilaç seçimini etkileyebileceği belirtilmektedir. Çalışmamızın dikkat çeken sonuçlarından biri, Stroop puanlarının, özellikle DEHB ve epilepsi olan kızlarda MPH tedavisi ile anlamlı bir değişiklik olmamasıdır. (*Anadolu Psikiyatri Derg* 2019; 20(6):642-650)

Anahtar sözcükler: Epilepsi, dikkat eksikliği hiperaktivite bozukluğu, cinsiyet, metilfenidat

INTRODUCTION

Attention deficit and hyperactivity disorder (ADHD) affects approximately 5-7% of children worldwide.¹ The most common type is ADHD combined type (ADHD-CT) which is followed by ADHD attentional deficit predominant type (ADHD-AD) and ADHD hyperactive-impulsive type (ADHD-HI).^{2,3}

Epilepsy and ADHD are common diseases during childhood and adolescence, and they have significant effects on the social, academic, and emotional development of the individual. Accompanying neuropsychiatric disorders are demonstrated in 40-70% of epileptic individuals.⁴ The most common of those neuropsychiatric disorders are ADHD, autism, depression, and anxiety disorders.^{5,6} ADHD is estimated to be present in 13-40% of epileptic children.⁷⁻¹¹ Among children with a history of recent onset seizures and epilepsy diagnosis, ADHD frequency is reported to be 2.5 times more than the expected frequency in the general population; the association is especially valid for ADHD-AD subtype which has a 3.7 times increased risk.¹² Similarly, epilepsy risk in cases with ADHD is 2.7 times higher than the general population and seizure frequency tends to increase in epileptic ADHD cases compared to non-ADHD epileptics.¹³ Among many hypotheses proposed to explain the association between ADHD and epilepsy, the leading ones are similar genetic vulnerabilities, similar pathophysiology as in frontal lobe epilepsy, subclinical epileptiform discharges and noradrenergic epileptiform discharges that play a role in the pathology of both disorder.¹⁴ Also, recurrent seizures and cognitive side effects of antiepileptic drugs may also cause or increase the severity of ADHD.⁷

Although long-term methylphenidate (MPH) administration has been believed to reduce seizure threshold in epileptic individuals for a long time and may trigger seizures, there are few short- and long-term studies on the effects of MPH treatment in patients with concurrent epilepsy

and ADHD diagnosis. Present studies report that MPH treatment of patients with ADHD and epilepsy is shown to positively affect the quality of life scores and to be safe and effective.^{9,15-19} and provides a significant improvement in ADHD symptoms.^{7,15-18,20-24} On the other hand, it is reported that MPH treatment may be related to aggravation of seizure frequency in subjects with ADHD and epilepsy.²⁴

In summary, not enough studies are available regarding the effects of ADHD and epilepsy comorbidity on clinical and attentional findings and variables that determine these effects. This study aimed to compare differences between ADHD children and adolescents with or without epilepsy according to the initial levels of inattention measured with the Stroop test and the levels of their MPH response with gender variability.

METHODS

Sample

This study included 94 children and adolescents with ADHD between 8-14 years range (mean age; 10.8±1.7). Forty-seven of them had epilepsy, and 47 did not. Diagnoses of psychiatric disorders were made after a clinical interview and evaluation by a child and adolescent psychiatrist in accordance with DSM-IV-TR criteria.²⁵ The two groups were matched one-by-one according to age, sex, education level, ADHD subtype, and comorbidities. Pervasive developmental disorder or mental retardation were exclusion criteria for both groups. In addition to minimizing the possibility of an active epileptic discharge affecting the attention measurement inclusion criteria also included not having a seizure for the last six months and using anti-epileptics at least for the last three months for the epilepsy group.

Psychometric measurements

Stroop TBAG Form: This test was used to determine attention deficit and to screen its

severity. It was developed by Stroop, and Turkish adaptation and standardization study was performed.²⁶⁻²⁸ In this study, initial attention functions and effects of MPH treatment on attention were evaluated with Stroop test TBAG form. In statistical analyses, Stroop total time (ST) and Stroop total error and correction (SEC) scores were used. Stroop form was applied three times recurrently for each case: at initial presentation (S-1); during the evaluation at the third month of MPH treatment 1-2 hours after MPH use (S-2); and after three days of drug holiday in cases who received MPH treatment for six months (S-3).

Conners Teacher Rating Scale (CTRS) and Conners Parent Rating Scale (CPRS): CTRS was developed by Conners,²⁹ and validity and reliability study for the Turkish version was performed by Sener et al.³⁰ CPRS was developed by Conners,²⁹ and validity and reliability study for the Turkish version was performed by Dereboy et al.³¹

Starting methylphenidate treatment and follow up

Before starting MPH to the patients, as a routine procedure of our clinic, electrocardiogram, hemogram, and routine biochemical evaluations were performed, and presence of an organic disorder that may be of concern for drug use was investigated. These measurements were repeated during follow up visits at three-month intervals after titration of the drug to the appropriate dose. The data of this study were obtained a chart review of the patients and approval was obtained from the ethics committee of Çukurova University Medical School. The cases and their families were informed about MPH use at the beginning of treatment. Expected benefits, possible side effects of, and reasons for the proposed treatment were explained. MPH-OROS treatments were planned (dose range: 18-72 mg/day, once a day, after breakfast).

Statistical analyses

The data were analyzed with SPSS 16.0 package program. Cross-tables and chi-square test were used for the analysis of categorical variables. Normal distribution of continuous variables was assessed with Shapiro-Wilk test. Analyses were made for comparisons of both mean Stroop scores of the two diagnostic groups between each other (between groups/independent variables) and between repeated measures of each group (intragroup/dependent variable) and the

non-parametric Mann-Whitney U test was used. Statistical evaluations of continuous variables in dependent groups were performed by the non-parametric Wilcoxon Signed Rank Test. Statistical significance was accepted as $p < 0.05$.

Sample size was calculated with an expected parameter estimate based on the study of Ayaz et al.³² Assuming 1 sided test a mean of 125.72 SRKT in group EG and a mean of 109.19 in Group NEG with a 31.7 standard deviation at baseline, the minimum sample size thus required to be approximately 47 in each study groups within a 95% confidence and 80% power.

RESULTS

Comparison of sociodemographic data

Each group included 30 (63.8%) males and 17 (36.2%) females. Each group included 38 (80.9%) cases with ADHD-CT and 9 (19.1%) cases with ADHD-AD. Evaluation of the distribution of the epileptic cases according to seizure type revealed that 10 (21.3%) cases had partial seizures; 22 (46.8%) cases had generalized seizures and 15 (31.9%) cases had paroxysmal activity disorder. Evaluation of the frequency of antiepileptic drugs revealed that 25 (80.9%) cases used valproate; six (12.8%) cases used carbamazepine, and 5 (6.3%) cases used other antiepileptics. None of the epilepsy cases receiving MPH-OROS treatment had a seizure during the six-month follow up period. Demographic data, developmental features, DEHB subtypes and comorbidities of the groups are given in Table 1.

The mean CTRS scores of both the epileptic and the non-epileptic males were significantly higher than those of females, but no difference was found between CPRS scores in terms of gender. Among epileptic cases, the mean CTRS and CPRS scores of ADHD-CT cases were higher than those of ADHD-AD cases. In the non-epileptic group, no difference was found in similar statistical analyses (Table 2).

Comparison of the groups with and without epilepsy

In a comparison of the Stroop scores of the two groups, the mean SEC-1 and SEC-3 scores of the ADHD cases with epilepsy were higher than those of the ADHD cases with epilepsy. No significant difference could be found between the mean ST-1, ST-2, ST-3, and SEC-2 scores of the epileptic and the non-epileptic groups.

Table 1. Clinical, demographic and developmental features according to the groups

	Epilepsy+ADHD		ADHD		Total	
	n	%	n	%	n	%
Total	47	50.0	47	50.0	94	100.0
Gender						
Male	30	63.8	30	63.8	60	63.8
Female	17	36.2	17	36.2	34	36.2
Attention deficit and hyperactivity disorder subtype						
Combined type	38	80.9	38	80.9	76	80.9
Attention deficit type	9	19.1	9	19.1	18	19.1
Co-morbidities						
Any co-morbidity	30	63.8	30	63.8	60	63.8
Disruptive behavior disorders	17	36.2	17	36.2	34	36.2
Anxiety disorders	11	23.4	11	3.4	22	23.4
Other disorders	2	4.3	2	4.3	4	4.3
Maternal age during delivery						
<25 age	22	46.8	24	51.1	46	48.9
25-35 age	23	48.9	21	44.7	44	46.8
>35 age	2	4.3	2	4.3	4	4.3
Delivery complications						
Yes	14	29.8	4	8.5	18	19.1*
No	33	70.2	43	91.5	76	80.9
Ability to start walking						
Normal time	39	83.0	43	91.5	82	87.2
>18 months	8	17.0	4	8.5	12	12.8
Ability to start speaking						
Normal time	30	63.8	31	66.0	61	64.9
>24 months	17	36.2	16	34.0	33	35.1

*: 0.009; Chi-square test, cross tabs analysis

Table 2. The mean CTRS and CPRS scores of the cases according to the diagnostic groups

	Epilepsy+ADHD (n=47) Mean±SD	ADHD(n=47) Mean±SD	Total (n=94) Mean±SD
Conners Teacher Rating Scale			
Total	30.9±14.1	30.0±11.7	30.5±12.9
Male	34.3±13.6	32.6±12.8	33.4±13.1
Female	25.0±13.4	25.4±8.0	25.2±10.9
p*	0.027	0.043	0.003
ADHD-CT	33.6±13.8	31.5±11.7	32.5±12.7
ADHD-AD	19.7±9.4	23.8±10.6	21.8±9.9
p*	0.007	0.110	0.002
Conners Parent Rating Scale			
Total	40.4±19.5	37.2±15.5	38.8±17.6
Male	43.1±17.6	37.8±14.5	40.4±16.2
Female	35.7±22.2	36.2±17.6	36.0±19.7
p*	0.191	0.756	0.242
ADHD-CT	43.7±18.9	39.4±15.4	41.5±17.3
ADHD-AD	26.6±16.2	28.0±13.1	27.3±14.3
p*	0.014	0.060	0.002

*: Mann Whitney U test; ADHD: Attention Deficit and Hyperactivity Disorder, -CT: Combined Type, -AD: Attention Deficit Type

Evaluation of the epileptic subgroups according to the mean Stroop scores

The mean Stroop scores, (ST-1, ST-2, ST-3, SEC-1, SEC-2, SEC-3) didn't change significantly according to the epilepsy subgroups. When the cases were grouped according to the anti-epileptic drug they use, an adequate number for statistical analysis couldn't be reached in any of the groups. Therefore, no comparison could be made according to the medications used.

Comparison of the groups according to the ADHD subtypes

No significant difference could be found between epileptic and non-epileptic ADHD subgroups according to ST-1 and SEC-1. Although all of the mean SEC-1, SEC-2 and SEC-3 scores were higher in the epileptic + ADHD-CT group compared with the non-epileptic + ADHD-CT group, statistical significance couldn't be found in any of the similar statistical analyses for the ADHD-AD

cases. Within-group comparisons of the epileptic cases according to ADHD subtypes revealed that the mean ST-3 and SEC-3 scores for ADHD-AD subtype were significantly higher than the ADHD-CT subtype, but no significant difference was found in similar analyses between the ADHD subtypes in non-epileptic cases (Table 3).

Comparison of the Stroop scores of the groups according to gender

Compared to the non-epileptic ones, SEC-3 scores of the epileptic males were higher, although no significant difference could be found in any of the comparisons between the Stroop scores of epileptic and non-epileptic females. The mean ST-1 score of the epileptic males was significantly higher than that of epileptic girls, no significant difference could be found between the mean Stroop scores of non-epileptic males and females (Table 3).

Table 3. Comparison of the Stroop scores recorded between, during and after treatment between the groups

	Stroop-ST		p*	Stroop-SEC		p*
	EG	NEG		EG	NEG	
Stroop-1						
Total	126.5±40.5	119.9±45.7	0.203	9.1±5.1	6.5±4.2	0.012
Male	134.8±44.3	124.5±53.7	0.094	10.1±5.3	7.3±4.5	0.415
Female	112.0±28.3	111.8±25.9	0.803	7.4±4.5	5.2±3.6	0.202
p**	0.049	0.674		0.089	0.127	
ADHD-CT	123.3±32.4	116.2±30.6	0.299	8.5±4.1	6.1±3.9	0.016
ADHD-AD	140.4±65.5	135.5±85.7	0.659	11.8±7.9	8.3±5.5	0.287
p**	0.570	0.968		0.166	0.377	
Stroop-2						
Total	101.0±26.3	97.1±39.9	0.336	4.3±1.4	3.2±3.6	0.061
Male	95.8±21.3	98.6±47.6	0.503	4.5±10.3	3.8±40.3	0.127
Female	121.5±44.5	94.7±25.7	0.324	3.5±2.1	2.3±2.3	0.483
p**	0.433	0.724		0.498	0.460	
ADHD-CT	100.0±27.7	92.1±26.7	0.349	4.2±1.4	2.6±3.0	0.041
ADHD-AD	1100±0.0	115.1±71.4	0.617	5.0±0.0	5.5±5.2	0.604
p**	0.384	0.674		0.470	0.079	
Stroop-3						
Total	102.8±33.7	91.2±27.0	0.324	7.4±5.7	2.6±2.1	0.004
Male	103.7±34.1	87.1±250.3	0.160	7.8±6.4	2.8±1.9	0.011
Female	99.0±45.2	96.7±30.0	0.793	5.5±2.1	2.5±2.5	0.143
p**	0.602	0.432		1.00	0.766	
ADHD-CT	90.7±25.2	93.2±28.1	0.976	4.8±2.1	2.6±2.2	0.024
ADHD-AD	151.0±1.4	80.3±20.5	0.083	17.5±3.5	3.0±1.7	0.076
p**	0.037	0.538		0.036	0.645	

p*: Mann-Whitney U test; Epileptic and Non-Epileptic intergroup comparison; p**: Mann-Whitney U test; analysis made separately for EG and NEG based on gender and ADHD subtypes (Intergroup comparison of independent variables)
EG: Epileptic Group; NEG: Non-Epileptic Group; ST: Stroop total time; SEC: Stroop Total Error+Correction Scores;
Stroop-1: Stroop scores recorded before the treatment; Stroop-2: The mean Stroop scores recorded during methylphenidate-OROS treatment; Stroop-3: The mean Stroop scores recorded after discontinuation of the treatment with methylphenidate-OROS which lasted for six months;
ADHD: Attention Deficit and Hyperactivity Disorder, -CT: Combined Type, -AD: Attention Deficit Type

In order to evaluate whether a change occurred among three Stroop measurements, comparisons were made between the two groups and within each group. To assess whether improvement happened in attention functions, the differences among the pretreatment (S-1), during treatment (S-2) and posttreatment mean Stroop

scores were evaluated. Accordingly, in the general group, all the differences between epileptic and non-epileptic males and ST-1/2, ST-1/3, SEC-1/2 and SEC-1/3 measurements in nonepileptic females were statistically significant. In epileptic girls none of such analyses was significant (Table 4).

Table 4. Change in the mean Stroop score during and after the treatment

	Total	p	Male	p	Female	p	ADHD-CT	p	ADHD-AD	p
Stroop										
ST 1/2										
Total	27.6±22.8	0.001	30.2±25.2	0.0001	22.8±17.2	0.002	24.1±18.5	0.0001	43.1±34.1	0.018
EG	32.1±23.1	0.005	35.0±24.4	0.012	20.5±17.6	0.180	27.8±20.1	0.008	-	-
NEG	26.1±22.9	<0.001	27.9±26.0	<0.001	0.6±2.2	0.004	22.6±18.1	<0.001	38.6±35.0	0.027
ST 1/3										
Total	22.4±17.1	<0.001	24.1±18.0	<0.001	19.2±15.6	0.012	23.6±16.9	<0.001	16.6±19.0	0.138
EG	25.6±22.9	0.017	28.6±23.7	0.025	13.5±20.5	0.655	29.8±21.5	0.017	8.5±27.5	0.655
NEG	20.7±13.5	<0.001	20.8±12.7	0.005	23.2±17.9	0.017	20.5±13.7	0.001	22.0±15.3	0.109
SEC 1/2										
Total	4.2±4.5	<0.001	4.6±5.2	<0.001	3.4±2.9	0.003	3.6±3.4	<0.001	7.1±7.6	0.027
EG	6.2±6.6	0.017	7.2±7.0	0.028	2.0±2.8	0.317	4.5±4.4	0.028	-	-
NEG	3.5±3.4	<0.001	3.4±3.8	0.002	3.7±2.9	0.005	3.2±2.9	<0.001	4.8±4.9	0.042
SEC 1/3										
Total	4.0±3.8	<0.001	4.2±4.2	0.001	3.7±3.3	0.010	4.0±3.7	<0.001	4.0±5.0	0.066
EG	5.3±3.9	0.008	5.2±4.2	0.018	5.5±3.5	0.180	5.7±4.1	0.018	3.5±3.5	0.180
NEG	3.3±3.7	0.001	3.4±4.2	0.020	3.2±3.3	0.027	3.1±3.3	0.003	4.3±6.6	0.180

p*: Wilcoxon Signed Rank Test; Comparison of measurements in EG+ADHD and NEG+ADHD groups at initial, during and post-treatment (Intergroup comparison of dependent variables)

EG: Epileptic Group, NEG: Non-Epileptic Group, ST: Stroop total time, SEC: Stroop Total Error+Correction

S-1/2: Comparison of mean stroop scores recorded at the baseline and during the treatment (as per time, error, correction)

S-1/3: Comparison of mean stroop scores recorded at the baseline and after the treatment (as per time, error, correction)

ADHD: Attention Deficit and Hyperactivity Disorder, -CT: Combined Type, -AD: Attention Deficit Type

DISCUSSION

This study showed that the effect of MPH treatment on Stroop scores change according to ADHD subgroups, gender, and presence of epilepsy. Accordingly, it can be concluded that ADHD-AD cases with epilepsy are significantly different than ADHD-CT cases with epilepsy regarding mean Stroop scores. Some authors believe that executive functions in ADHD cases without epilepsy are affected more in attention deficit subtype than the combined type and these cases consist a subgroup with a different clinical appearance.^{33,34}

It was reported that the most common subtype was ADHD-CT subtype with a rate of 43.7%, and this was followed by ADHD-HI (37.5%) and ADHD-AD (18.7%) subtypes in epileptic ADHD children.³⁵ Similarly, ADHD-CT was the most common type in our study, and it was at a higher rate (80.9%) than current studies.^{24,35} In addition, there are also studies that reported ADHD-AD

subtype was more common in cases with epilepsy.^{36,37} The difference between this study and the previous ones regarding subtype rates may be related to many factors such as differences in sample and research methods.

Psychiatric comorbidities are common (37-77%) in epileptic children and adolescents.³⁸ Similarly, in our study, rate of psychiatric diagnosis accompanying epilepsy+ADHD cases is 63.8%. Besides ADHD, the most common diagnosis was disruptive behavioral disorder (36.2%), followed by anxiety disorders (23.4%) and other disorders (4.3%). Our findings are consistent with previous studies which demonstrated that the frequency of other psychiatric comorbidities in epileptic children with ADHD was similar with nonepileptic ADHD children.³⁹

MPH use and seizure risk

Methylphenidate is effective in most of the children and adolescents with ADHD symptoms and comorbid epilepsy without increasing seizure

risk significantly,^{7,15,17,19,23,40} but the number of controlled studies are limited.^{19,40} Current studies state that stimulants seem safe for ADHD treatment in children with epilepsy needs support from large population-based studies.^{23,41} In a prospective observational study, the seizure recurrence rate was not significantly different between patients who were treated with MPH or those who did not get any specific pharmacological intervention for ADHD.¹⁸ The absence of seizures in any of the epileptic cases in our study also supports these findings.

Differences between genders

It is very interesting that in this study no difference was observed in epileptic females in ST or SEC scores at the beginning, during and after cessation of MPH treatment. Similarly, no significant difference was observed in the epilepsy + ADHD-AD group in ST1/2, ST 1/3, SEC- 1/2 and SEC 1/3 scores during MPH treatment and after cessation. On the other hand, in all of the measurements in the epilepsy + ADHD-CT group, there were significant decreases, which means a positive response to medication. The more common occurrence of ADHD-AD subtype in females may have affected the results of these two analyses. Although ADHD-CT subtype was the predominant type in non-epileptic cases, ADHD-AD subtype was two times more common in females than in males.² Selective attention was more commonly affected in girls with ADHD and boys gave more impulsive responses in continuous attention tasks.

Most of the information on the differences in MPH treatment response between genders is based on animal studies and usually appears to focus on neurotransmitter effects. It was proposed that in addition to effects of sex hormones

on MPH pharmacokinetics, estrogen might mediate some effects of psychostimulants by affecting mRNA expression in dopamine and serotonin receptors in the brain.⁴² GABAergic system related behavioral activation due to the repeated psychostimulant application is more prominent in females and mediated by reproductive hormones.⁴³ Behavioral activation due to MPH application may decrease the curative effect of MPH in girls, and smaller doses may improve attention functions more effectively without inducing disruptive effects.⁴⁴

Brown et al. found that MPH treatment response in gender-specific differences may be related to striatal Brain-Derived Neurotrophic Factor (BDNF).⁴⁵ The effect of gender in ADHD is probably on clinical appearance and other comorbid psychiatric disorders.² It is not yet clear whether attention deficit in cases with epilepsy is due to disease subtype or gender in cases comorbid with epilepsy.

CONCLUSION

The strengths of our study are a one-to-one match for subtypes of the epileptic and non-epileptic ADHD, gender, and psychiatric comorbidities, adequate patient number, and the absence of any seizures during the MPH use period. It is noted that the co-occurrence of ADHD and epilepsy may affect the treatment choices and the clinical courses of both diseases. Therefore, It is recommended that regular follow-up is necessary for drug interactions, clinical observation and rating scales, the presence/absence of seizures and their frequency, and the clinical severity of ADHD in patients ADHD.

Authors' contributions: P.Ç.R.: data collection, literature, writing manuscript; G.G.Ç.: finding topic, literature, data collection, writing manuscript; A.Y.T.: planning, data collection, statistics, writing manuscript; İ.S.G.: literature, writing manuscript; Ö.M.H.: examination sample.

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