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RESEARCH

Association between attention deficit hyperactivity disorder and chronotype in adults with epilepsy

Epilepsi tanılı yetişkinlerde dikkat eksikliği ve hiperaktivite bozukluğu ile kronotip arasındaki ilişki

Kerim Uğur[1], Tunahan Sun[2], İrem Taşçı[3], Fatma Kartal[4]

[1]Turgut Özal University, Malatya, Türkiye
[2]Düziçi State Hospital, Osmaniye, Türkiye
[3]Fırat University, Elazığ, Türkiye
[4]Kırıkkale University, Kırıkkale, Türkiye

Abstract

Purpose: This study aimed to determine the chronotype characteristics in adults with epilepsy, examine the relationship between chronotype and Attention Deficit Hyperactivity Disorder (ADHD), and compare ADHD symptom levels between patients with epilepsy and healthy controls.

Materials and Methods: The study included 90 patients with epilepsy and 70 healthy controls, aged between 18 and 65 years. Sociodemographic and clinical data (seizure status, EEG, and MRI findings) were collected from the participants. The Morningness-Eveningness Questionnaire (MEQ), Adult ADHD Diagnosis and Evaluation Inventory, and Adult ADHD Self-Report Scale (ASRS) were administered.

Results: A higher proportion of intermediate chronotypes was observed in the epilepsy group (68.9%) than in the control group (51.4%). ADHD symptom scores were higher in patients than in controls. Among patients with epilepsy, individuals with intermediate and evening chronotypes had significantly higher ADHD symptoms than those with morning chronotype. Although individuals with an evening chronotype had higher ADHD symptom levels than those with an intermediate chronotype, this difference was not statistically significant.

Conclusion: The findings suggest that ADHD symptoms become more pronounced in patients with epilepsy as chronotype characteristics shift toward eveningness. Circadian features should be considered in the evaluation and management of ADHD comorbidity in adult patients with epilepsy.

Keywords:. Adult epilepsy; ADHD , evening chronotype; circadian rhythm; neuropsychiatric comorbidity

Öz

Amaç: Bu çalışmanın amacı, epilepsi tanılı yetişkin bireylerde kronotip özelliklerini belirlemek, kronotip ile Dikkat Eksikliği ve Hiperaktivite Bozukluğu (DEHB) arasındaki ilişkiyi incelemek ve epilepsi hastaları ile sağlıklı kontroller arasında DEHB belirti düzeylerini karşılaştırmaktı.

Gereç ve Yöntem: Çalışmaya 18-65 yaş arası 90 epilepsi tanılı hasta ve 70 sağlıklı kontrol dahil edildi. Katılımcıların sosyodemografik ve klinik verileri (nöbet durumları, EEG ve MR bulguları) toplandı. Sabahçıl-Akşamcıl Anketi (MEQ), Erişkin DEHB Tanı ve Değerlendirme Envanteri ve Erişkin DEHB Öz Bildirim Ölçeği (ASRS) uygulandı.

Bulgular: Epilepsi grubunda ara kronotip oranı (%68.9), kontrol grubuna (%51.4) göre daha yüksekti. DEHB belirti puanları epilepsi hastalarında sağlıklı kontrollerden anlamlı düzeyde daha yüksekti. Epilepsi hastaları arasında, sabahçıl kronotipe sahip bireylerle karşılaştırıldığında, ara ve akşamcıl kronotipe sahip bireylerin DEHB belirtileri anlamlı düzeyde daha yüksekti. Akşamcıl kronotipe sahip bireylerin DEHB belirti düzeyleri, ara kronotipe göre daha yüksek olsa da bu fark istatistiksel olarak anlamlı değildi.

Sonuç: Bulgular, DEHB belirtilerinin epilepsi hastalarında kronotip özellikleri akşamcıl yöne kaydıkça daha belirgin hale geldiğini göstermektedir. Bu durum epilepsi tanılı erişkin hastalarda DEHB komorbiditesinin değerlendirilmesi ve yönetiminde sirkadiyen özelliklerin göz önünde bulundurulması gerektiğini göstermektedir.

Anahtar kelimeler: Erişkin epilepsi; DEHB, akşam kronotipi; sirkadiyen ritim; nöropsikiyatrik komorbidite

Address for Correspondence: Tunahan Sun, Düziçi State Hospital Department of Psychiatry, Osmaniye, Türkiye
E-mail: tunasun01@gmail.com
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INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by a persistent tendency to experience recurrent epileptic seizures, encompassing a wide range of syndromes and seizure types[1]. Sleep quality and duration are recognized as triggers of seizure activity in several epilepsy subtypes. For instance, insomnia is known to provoke myoclonic and generalized tonic-clonic seizures in juvenile myoclonic epilepsy (JME), whereas specific electroencephalography (EEG) abnormalities, such as continuous spike-wave discharges, tend to occur specifically during sleep in certain syndromes[2,3].

The temporal distribution of epileptic seizures has long been associated with circadian rhythms. Some authors have suggested that seizure occurrence may follow a 24-hour biological rhythm, depending on the type of epilepsy[4]. This has led to increased interest in chronotype, which refers to an individual's circadian preference for activity classified as morning, intermediate, or evening and is influenced by both internal and environmental factors[5]. Although the relationship between chronotype and seizure timing has been studied, a gap still exists in understanding its association with neuropsychiatric comorbidities in epilepsy.

Cognitive and behavioral impairments are common in epilepsy, but attention deficits have received comparatively less attention[6]. Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by inattention, impulsiveness, and hyperactivity, which often persists into adulthood. Adult ADHD is estimated to affect approximately 2–5% of the general population[7]. Although studies in pediatric populations with epilepsy have consistently reported higher rates of ADHD than controls, research on adult patients with epilepsy (PWE) remains limited. Emerging evidence suggests that approximately 20% of adult PWE exhibit ADHD symptoms associated with psychosocial difficulties and reduced quality of life[9].

Recent research has revealed a strong association between evening chronotypes and ADHD symptoms in non-epileptic populations[10]. However, the relationship between chronotype and ADHD remains underexplored in adult PWE populations.

Given the limited research on the clinical significance of ADHD comorbidity in adult PWE, this study aimed to (1) determine chronotype characteristics in adult PWE, (2) examine the relationship between chronotype and ADHD symptoms, and (3) compare ADHD symptom levels between PWE and healthy controls (HC). We hypothesized that chronotype in PWE is associated with ADHD symptoms and that chronotype distribution differs between PWE and HC. A better understanding of chronotype traits in adult PWE with ADHD may offer valuable insights into clinical practice and future research.

MATERIALS AND METHODS

Sample

Ethics committee approval was obtained for this study from the Malatya Turgut Özal University Clinical Research Ethics Committee, as per their decision dated 05/28/2021, number 2021/33. Patients who visited the neurology outpatient clinic at Malatya Turgut Özal University Training and Research Hospital between 06/01/2021 and 06/01/2022 and were diagnosed with epilepsy by a senior neurologist (third author, associate professor), as well as healthy individuals serving as the control group, were included in the study.

The inclusion criteria for the study were as follows: participants needed to be between 18 and 65 years old, literate and capable of completing self-report scales, and free of any diagnosis of comorbid neurological disorders or major psychiatric conditions, including schizophrenia, bipolar disorder, major depressive disorder, and substance use disorder. Individuals with delirium, dementia, or intellectual disabilities that may impair cognitive functioning were also excluded.

The patient group included 97 adult PWE who had not taken antiepileptic drugs for at least three months. To avoid potential confounding effects of pharmacological treatment, only patients who had not taken anti-epileptic drugs (AEDs) for at least the past three months were included in the study. This decision was based on prior evidence that certain AEDs may affect attention, executive functioning, or behavioral regulation, which could interfere with the accurate assessment of ADHD[11]. Of the 90 patients in the group, 42 had been seizure-free for at least 2 years and had stopped their antiepileptic treatment based on the criteria outlined in the epilepsy diagnosis and treatment guide published by the Turkish

Neurology Society Epilepsy Study Group[12]. The remaining 48 patients discontinued their antiepileptic medications on their own due to treatment incompatibility. Seven patients with symptomatic and cryptogenic epilepsy, cardiac issues, renal failure, hepatic failure, electrolyte imbalances, active infections, and fever were excluded from the study.

We included 90 healthy volunteers who met the inclusion criteria and matched the patient group in terms of age and sex as the control group. HC were recruited through announcements issued within the university and hospital settings. The volunteers included university staff, students, and family members of patients. Additionally, individuals who presented to the neurology outpatient clinic but did not receive a neurological diagnosis, had no history of psychiatric illness, and did not report any psychiatric symptoms were also included. All participants in the HC group were screened by both a neurologist and psychiatrist to confirm eligibility. HC were matched with the patient group based on age and sex. Participants in both groups did not receive monetary or material compensation. Participation was voluntary. Eleven participants who filled out the scales without understanding and nine participants with a history of psychotic disorder, bipolar disorder, major depressive disorder, and alcohol and substance use disorder according to the DSM-5 were excluded from the study. We continued the study with 90 adult PWE and 70 HC.

An a priori power analysis was conducted using GPower 3.1 software based on a two-tailed independent samples t-test. The parameters were set as follows: $\alpha = 0.05$, power $(1–\beta) = 0.85$, medium effect size (Cohen's $d = 0.5$), and an allocation ratio (control/patient) of 0.78. Based on these parameters, the minimum required sample size was calculated to be 83 participants in one group and 65 in the other, for a total of at least 148 participants. In the present study, 90 PWE and 70 HC were included, indicating that the sample size was sufficient to detect medium-sized differences between groups.

Procedure

All patients and HC provided informed consent to participate in the study. Sociodemographic data of the patients and HC were collected using a form. Participants' medications and comorbidities were also recorded. Additionally, electrophysiological and radiological data including EEG findings, MRI results, and seizure status were collected for patients.

All participants underwent a standardized neurological examination conducted by the same senior neurologist (third author, associate professor) to confirm the diagnosis of epilepsy and rule out other neurological disorders. Epilepsy was diagnosed based on the revised criteria of the International League Against Epilepsy[1]. 1) Those who had two provoked seizures within more than 24 hours. 2) Those who have had one unprovoked seizure and possess a 60% or higher risk of experiencing another seizure within the next 10 years (conditions that increase seizure risk include a) nocturnal seizure, b) late symptomatic seizure, c) seizure-related lesion on radiological imaging, and d) epileptic discharges on EEG). 3) Individuals whose seizure semiology and age group matched those of an epileptic syndrome. Individuals meeting any of these three criteria are diagnosed with epilepsy.

The neurologist confirmed the diagnoses based on the clinical history, seizure semiology, EEG findings, and, when available, neuroimaging results. Additionally, each participant was assessed by a senior psychiatrist (first author, associate professor) through clinical interviews based on the DSM-5 diagnostic criteria to rule out major psychiatric disorders, including schizophrenia, bipolar disorder, major depressive disorder, and substance use disorders.

EEG protocol: PWE underwent EEG using the 21-electrode bipolar and reference montage formats of the international 10-20 system, recorded with a Nihon Kohden Neurofax EEG-1200 system (Nihon Kohden Corporation, Tokyo, Japan). EEG recordings were performed by a trained EEG technician at the EEG laboratory of the study center and were subsequently interpreted and reported by the same neurologist.

All recordings were conducted between 8:00 a.m. and 5:00 p.m. on weekdays, corresponding to the routine working hours of the EEG unit. In addition, to rule out cryptogenic and symptomatic epilepsy, we retrospectively reviewed the epilepsy-protocol brain MRI scans routinely performed at the time of diagnosis.

The patients and HC were referred to a psychiatrist for psychiatric evaluation. The Morningness-Eveningness Questionnaire (MEQ), Adult ADHD Diagnosis and Evaluation Inventory, and Adult ADHD Self-Report Scale (ASRS) were administered to the participants by a psychiatrist.

Electrophysiological and radiological data

EEG findings were defined based on the presence or absence of epileptiform discharges, as assessed by a neurologist. MRI findings were evaluated based on radiology reports to determine whether structural brain lesions potentially responsible for the observed seizure semiology were present. Seizure status was defined based on whether the patient continued to experience epileptic seizures, as determined by clinical follow-up and medical history.

Measures

Sociodemographic Data Form

The semi-structured sociodemographic data form, created by the authors, included information on age, gender, marital status, educational level, employment status, monthly income, and the presence of psychological problems in childhood. The presence of psychological problems in childhood was assessed using a single self-report item in the sociodemographic data form, asking participants whether they had ever experienced emotional or behavioral problems during childhood that required professional help or caused significant functional impairment. Additionally, when relevant, this information was confirmed by reviewing the hospital's electronic medical record system for documented psychiatric diagnoses or treatments during childhood.

The Morningness-Eveningness Questionnaire (MEQ)

This scale was developed by Horne and Östberg (1976)[13]. The scale consists of 19 questions that question people about their lifestyle, sleep-wake patterns and performance. This is a self-report evaluation scale. The chronotype characteristics of individuals were determined according to the total score obtained at the end of the survey. A total score of 16-41 is classified as "evening," 42-58 as "intermediate," and 59-86 as "morning." A reliability study of the Turkish version of the survey was conducted in 2005. Cronbach's α values were 0.785 and 0.812 for the 1st and 2nd applications, respectively, and the test-retest reliability coefficient was 0.84[14].

The Adult ADHD Diagnosis and Evaluation Inventory

This scale was developed in 1995 by Prof. Dr. Atilla TURGAY in Canada for the diagnosis of adult ADHD. It is a five-point Likert-type rating scale. It consists of three sub-sections. The first section (Turgay 1) focuses on attention deficit, including nine items related to symptoms of attention deficit according to the DSM-IV. Turgay 1 evaluates symptoms such as distractibility, forgetfulness, and difficulty maintaining attention. The second section (Turgay 2) contains the criteria for hyperactivity/impulsivity symptoms in the DSM-IV and includes nine items. Turgay 2 evaluates behaviors such as restlessness, interrupting others, and acting without hesitation. The third section (Turgay 3) covers the characteristics of ADHD and related issues. The Turgay 3 evaluates ADHD-related features and functional impairments in academic, social, and occupational domains. Form opinions based on clinical experience and observations. This section included 30 items. Cronbach's alpha was 0.9566 for the internal consistency coefficients to assess the overall reliability of the scale[15].

The Adult ADHD Self-Report Scale (ASRS)

This scale is a standard assessment tool developed by the World Health Organization for screening mental disorders[16,17]. The scale includes symptoms related to ADHD, in line with the DSM-IV-TR diagnostic criteria. The scale consists of two parts: Part A contains six items with high predictive power for ADHD symptoms, and Part B includes 12 items. The scale is designed to assess how frequently individuals have experienced symptoms over the past six months; responses are rated from "never" to "very often" and scored between 0 and 4. Validity and reliability studies of the Turkish-adapted version of the scale were conducted[17].

Statistical analysis

The SPSS 25 statistics program was used for data analysis. The normality of the data was assessed by examining the skewness and kurtosis values. The fact that the skewness and kurtosis values were within the range of ±2 supports that the data were normally distributed. After confirming that the normal distribution assumption was met, descriptive statistics (frequency, percentage, and mean), t-tests for independent samples, and one-way analyses of variance (one-way ANOVA) were conducted. Pearson's correlation analysis and chi-square tests were used for data analysis. An independent sample t-test was applied to compare paired groups, and a one-way ANOVA was employed to compare the

means of three or more groups. The relationship between categorical variables was assessed using the chi-square test. For categorical variables with significant results (e.g., education level, occupational status, monthly income, and chronotype distribution), post hoc pairwise comparisons were performed using the Bonferroni correction to control for multiple testing. For comparisons of mean scores across chronotype groups (e.g., ADHD symptom scores), a one-way ANOVA was followed by Tukey's Honestly Significant Difference (HSD) test as a post hoc analysis. Linear relationships between variables were examined using Pearson's correlation coefficient. Statistical significance was set at $P < 0.05$.

RESULTS

Table 1 presents a comparison of the sociodemographic characteristics of the participants in the patient and healthy control groups. The groups differed significantly in terms of educational level ($p < 0.001$), occupational status ($p < 0.001$), and monthly income ($p = 0.001$), while they were similar in terms of gender, marital status, childhood history of psychological problems, and mean age. Post hoc analyses with Bonferroni correction indicated that the proportion of participants who were unemployed, retired, or housewives was significantly higher in the patient group than in the HC group. These differences explain the overall significant variation observed in occupational status. Similarly, lower education levels and monthly income were more commonly observed in the patient group, explaining the overall significant differences between the groups.

Patients were divided into nine subgroups based on seizure type: primary generalized tonic-clonic seizures, absence seizures, myoclonic seizures, generalized tonic-clonic seizures with myoclonic seizures, partial seizures with impaired awareness, partial seizures with preserved awareness, focal to bilateral tonic-clonic seizures, focal motor seizures, and visual seizures. When seizures were broadly classified as focal or generalized, 63 patients were identified with generalized epilepsy, and 27 patients had focal epilepsy. Subgroup analysis was not possible because of the uneven numbers in each group. The number of patients according to seizure type is shown in Table 2.

Table 3 shows the chronotype distributions of the participants by group. It was found that 68.9% of the patients and 51.4% of the HC were of intermediate type. Chronotype distribution differed significantly between the groups ($p < 0.05$). Post hoc analysis using the Bonferroni correction revealed that the intermediate chronotype was significantly more prevalent in the patient group than in the morning and evening types, accounting for the observed difference in chronotype distribution between the groups.

The mean scores of the groups on the scales are presented in Table 4. The mean scores of the patient group were higher than those of the healthy group, and a statistically significant difference was observed ($p < 0.001$).

Table 5 presents the scores of the patient group based on chronotype, duration of illness, seizure status, and EEG and MRI findings. The difference between the ASRS and Turgay 1 and 2 scores of the patients according to chronotype was not significant ($p > 0.05$). A one-way ANOVA revealed a significant difference in Turgay 3 scores across chronotypes ($F = 3.764$, $p = 0.027$). Post hoc comparisons using Tukey's HSD test indicated that individuals with evening and intermediate chronotypes exhibited significantly higher Turgay 3 scores than those with a morning chronotype ($p < 0.05$). The difference between the mean scores obtained from the scales based on the duration of the disease, EEG findings, and seizure status of the patients was not significant. Although the difference in mean scores between the ASRS and Turgay 1 and 2 scales and the presence of MRI findings was not significant, the Turgay 3 scores of patients without MRI findings were significantly higher than those with MRI findings ($p < 0.05$).

The relationships between age, disease duration, EEG findings, MRI findings, and scale scores in the patient group are presented in Table 6. There was a weak but significant correlation between age and MRI findings ($r = 0.245$, $p = 0.020$), illness duration ($r = 0.301$, $p = 0.004$), and Turgay 3 scores ($r = –0.259$, $p = 0.014$). A moderate and significant correlation was observed between the ASRS total scores and both Turgay 1 and 2 scores ($r = 0.534$, $p < 0.001$), as well as Turgay 3 scores ($r = 0.397$, $p < 0.001$). Additionally, a weak but significant negative correlation was found between Turgay 3 scores and chronotype scores ($r = –0.277$, $p = 0.008$).

Table 1. Sociodemographic characteristics of participants

Characteristics	Group		Statistical test	p-value
	Patient n (%)	Control n (%)		
Mean age (Mean ± SD)	33.13±11.82	34.50±11.74	t: -0.727	0.468
Gender				
Male	47 (52.2)	33(47.1)	X^2: 0.406	0.524
Female	43 (47.8)	37(52.9)		
Marital status				
Married	35(38.9)	36(51.4)		
Single	51(56.7)	30(42.9)	X^2: 3.005	0.223
Divorced	4(4.4)	4(5.7)		
Education level*				
Primary school	16(17.8)	4(5.7)		
Middle School	8(8.9)	5(7.1)	X^2:40.687	<0.001
High school	38(42.2)	5(7.1)		
University	28(31.1)	56(80)		
Occupational status*				
Employed	43(47.8)	43(61.4)		
Unemployed	13(14.4)	1(1.4)	X^2:25.250	<0.001
Student	10(11.1)	21(30)		
Housewife	19(21.1)	5(7.1)		
Retired	5(5.6)	0(0)		
Monthly income*				
Very low income level	25(27.8)	8(11.4)	X^2: 14.153	0.001
Low income level	10(11.1)	1(1.4)		
Moderate income level	55(61.1)	61(87.1)		
Presence of psychological problems in childhood				
Yes	7(7.8)	3(4.3)	X^2:0.819	0.365
No	83(92.2)	67(95.7)		

t: Independent group t test, X^2: Chi-squared analysis;SD: Standard Deviation; *****: Post hoc analyses with Bonferroni correction revealed that the patient group included significantly more unemployed individuals, retirees, and housewives than the control group, contributing to the overall group difference in occupational status. Additionally, lower levels of education and monthly income were more common in the patient group, contributing to the observed group differences in these variables.

Table 2. Epilepsy subtypes in the patient group

Epileptic Seizure Subtype	Number of patients
Generalized Epilepsy	*63*
Primary generalized tonic-clonic seizures	54
Absence seizures	2
Myoclonic seizures	1
Generalized tonic-clonic seizures accompanied by myoclonic seizures	6
Focal Epilepsy	*27*
Partial seizures with awareness	8
Partial seizures without awareness	2
Focal to bilateral tonic-clonic seizures	12
Focal motor seizures	4
Visual seizures	1

Table 3. Chronotype distribution by group

Chronotype	Patient n (%)	Control n (%)	Statistical test	p-value
Morning type	23 (25.6)	24 (34.3)	X^2: 6.183	0.045
Intermediate type	62 (68.9)	36 (51.4)		
Evening type	5 (5.6)	10 (14.3)		

X^2: Chi-squared analysis.; Post-hoc comparisons using Bonferroni correction indicated that the intermediate chronotype was significantly more common in the patient group than in the control group.

Table 4. Comparison of ADHD scale scores between groups

Scale	Patient Mean ± SD	Control Mean ± SD	Statistical test	p-value
ASRS	31.31±10	10.55±5.14	t: 15.797	<0.001
Turgay 1 and 2	23.97±8.27	6.48±5.03	t: 15.577	<0.001
Turgay 3	30.97±13.28	9.42±6.35	t: 12.495	<0.001

t: Independent group t-test; SD: Standard Deviation, ASRS: The Adult ADHD Self-Report Scale, Turgay 1 and 2: Sections 1 and 2 of the Adult ADHD Diagnosis and Evaluation Inventory based on DSM-IV, developed by Turgay, Turgay 3: Sections 3 of the Adult ADHD Diagnosis and Evaluation Inventory based on DSM-IV, developed by Turgay

Table 5. Scale scores of patients by chronotype, disease duration, seizure status, EEG, and MRI

Variables		ASRS	Turgay 1 and 2	Turgay 3
Chronotype	Morning type[a] Mean ± SD	30.43±10.51	23.08±8.71	24.82±10.92
	Intermediate type[b] Mean ± SD	31.53±10.13	24.12±8.43	32.77±13.32
	Evening type[c] Mean ± SD	32.60±6.69	26.20±3.34	37±15.92
	Statistical test	F: 0.142	F: 0.319	F: 3.764
	p-value	0.868	0.728	0.027
				c,b>a**
Duration of illness	Less than 10 years	32.97±10.19	25.45±8.50	32.15±13.30
	More than 10 years	29.56±9.61	22.43±7.83	29.75±13.31
	Statistical test	t: 1.631	t: 1.753	t: 0.856
	p-value	0.106	0.083	0.394
EEG findings*	No	30.09±8.96	22.21±8.45	29.25±12.52
	Yes	31.98±10.55	24.94±8.08	31.93±13.70
	Statistical test	t: -0.856	t: -1.508	t: -0.915
	p-value	0.394	0.135	0.363
MRI findings†	No	30.60±9.41	23.22±8.38	33.46±13.99
	Yes	32±10.95	25.25±7.18	16.50±8.58
	Statistical test	t: -0.282	t: -0.467	t: 2.371
	p-value	0.779	0.642	0.022
Seizure status‡	No	30.91±10.34	24.52±8.68	27.92±12.71
	Yes	31.57±9.86	23.61±8.05	32.98±13.40
	Statistical test	t: -0.304	t: 0.513	t: -1.773
	p-value	0.762	0.609	0.080

F: One-way ANOVA, t: Independent group t test, *: Presence of epileptiform discharges on EEG, †: Presence of structural brain lesions related to seizure semiology, ‡: Presence or absence of ongoing epileptic seizures, **:** Post hoc comparisons using Tukey's HSD test
SD: Standard Deviation, EEG: Electroencephalogram, MRI: Magnetic Resonance Imaging

Table 6. Correlations between clinical variables and ADHD scores

		Age	EEG findings	MRI findings	Duration of illness	ASRS	Turgay 1 and 2	Turgay 3	MEQ
Age	r	1	-.106	.245*	.301**	-.011	.015	-.259*	.034
	P		.320	**.020**	**.004**	.921	.889	**.014**	.752
EEG findings†	r		1	.085	-.063	.091	.159	.097	.018
	P			.425	.556	.394	.135	.363	.868
MRI findings‡	r			1	.181	.070	.087	-.143	-.048
	P				.088	.512	.415	.179	.653
Duration of illness	r				1	-.171	-.184	-.091	.009
	P					.106	.083	.394	.936
ASRS	r					1	.534**	.397**	-.057
	P						**.000**	**.000**	.593
Turgay 1 and 2	r						1	.400**	-.082
	P							.000	.443
Turgay 3	r							1	-.277**
	P								**.008**
MEQ	r								1
	P								

Pearson correlation test *: Correlation is significant at the 0.05 level (2-tailed), **: Correlation is significant at the 0.01 level (2-tailed), †: Presence of epileptiform discharges on EEG, ‡: Presence of structural brain lesions related to seizure semiology
EEG: Electroencephalogram, MRI: Magnetic Resonance Imaging, ASRS: The Adult ADHD Self-Report Scale, Turgay 1 and 2: Sections 1 and 2 of the Adult ADHD Diagnosis and Evaluation Inventory based on DSM-IV, developed by Turgay, Turgay 3: Section 3 of the Adult ADHD Diagnosis and Evaluation Inventory based on DSM-IV, developed by Turgay, MEQ: The Morningness-Eveningness Questionnaire

DISCUSSION

Unlike most previous studies that mainly focused on pediatric populations or ignored circadian preferences, the present study examined the relationship between chronotype and ADHD symptoms in adult PWE. The most important finding of the present study is that individuals with evening and intermediate chronotypes exhibited significantly higher ADHD-related characteristics and problems (as reflected in the Turgay 3 scores) than those with the morning chronotype. Although the Turgay 3 scores were higher in the evening group than in the intermediate group, this difference did not reach statistical significance. Furthermore, chronotype scores were negatively correlated with ADHD symptom severity, indicating that a preference for eveningness may be linked to higher levels of inattention, hyperactivity, and impulsivity in this population. Most studies examining chronotype or circadian rhythm have found that adults with ADHD mainly exhibit evening chronotype. For instance, Michielsen et al. reported that nurses with ADHD were more likely to exhibit nocturnal chronotypes than their non-ADHD peers[18]. Similarly, eveningness has been linked to inattention symptoms in general adult populations[10], as well as to elevated ADHD symptoms in adolescent samples from both clinical and non-clinical groups[19]. Although previous research on chronotype and ADHD has primarily focused on individuals without epilepsy, our findings demonstrate that this association also exists in adult PWE. These findings suggest that evening chronotype preferences may exacerbate neurocognitive deficits, particularly in individuals with concurrent neurological disorders such as epilepsy, as evening chronotype has been associated with altered cortical excitability, reduced neuroplasticity, and impaired attention and working memory in neuroimaging studies[20].

In the present study, most adult PWE were classified as intermediate chronotype (68.9%), followed by morning (25.6%) and evening types (5.6%), which differed significantly from the HC group. This pattern aligns with recent reviews indicating the predominance of intermediate chronotypes in epilepsy populations. Similar results were found in a study on adults with JME (intermediate chronotype %49), although that study reported a higher proportion of evening types (41%) than morning types (10%)[21]. By contrast, other studies have found either a higher prevalence of morning types among adult PWE[22], or a greater frequency of evening types in specific epilepsy subtypes[23]. Pediatric studies have also yielded conflicting findings[24]. These

discrepancies may be due to differences in epilepsy subtypes, age groups, and chronotype assessment tools. More importantly, these differences suggest that circadian regulation of epilepsy may be heterogeneous in nature. Given that chronotype is influenced by neurobiological, environmental, and behavioral factors, PWE are likely to exhibit clinically relevant individual differences rather than a uniform chronotype profile[25]. This highlights the importance of personalized chronotype assessments in PWE.

Prior studies have indicated that ADHD and epilepsy may share common neurobiological mechanisms. For example, Wu et al. reported that ADHD is genetically linked to epilepsy, potentially due to shared pathogenic regions and tissue origin[26]. In the present study, attention deficit, hyperactivity, impulsivity levels, and ADHD-related characteristics and problems were significantly higher in PWE than in HC. Most of the existing literature has focused on pediatric populations, indicating that children with epilepsy have higher rates of attention problems and ADHD diagnoses than HC. For example, in a comparative study, children with temporal lobe epilepsy performed worse than those with idiopathic generalized epilepsy and HC on attention control tests, while no significant differences were found in other attentional domains[27]. Moreover, ADHD prevalence appears to vary by epilepsy severity, with up to 70% in children with drug-resistant epilepsy compared to 12–39% in newly diagnosed cases[28]. The relationship between epilepsy and ADHD is bidirectional, with each disorder increasing the risk of the other over time[29]. Despite these findings, little is known about this association in adults. The present study contributes to this underexplored area by demonstrating that adult PWE exhibit significantly higher levels of inattention, hyperactivity/impulsivity, and ADHD-related behavioral difficulties than HC.

Neuroimaging studies have provided valuable insights into the structural correlates of comorbid ADHD in PWE[30]. In the present study, ADHD-related traits were significantly more prominent in PWE without detectable epileptogenic lesions on MRI than in those with such lesions. This unexpected result may reflect the complexity of brain-behavior relationships, in which functional deficits may not always correspond to gross structural abnormalities[31]. Furthermore, our analysis relied on binary classifications (presence or absence of epileptogenic lesions) without including detailed lesion localization or volumetric measurements, which may have limited the detection of subtle or region-specific effects. Previous studies have produced mixed results. For example, one pediatric study found increased gray matter volume in the frontal regions and decreased brainstem volume in children with comorbid epilepsy and ADHD[32]. Another study by Saute et al. reported reduced cortical thickness in the frontal, parietal, and temporal lobes, along with decreased subcortical volumes of the caudate nucleus, thalamus, hippocampus, and brainstem in children with epilepsy and ADHD compared to HC[33]. This discrepancy may be explained by the structural and functional changes in the brains of children with ADHD associated with various higher-level cognitive functions[34]. Whether a specific anatomical or morphological phenotype characterizes the comorbidity between epilepsy and ADHD remains controversial, highlighting the need for further research.

Mahmoud et al. found that intellectual deficits in ADHD may be linked to epileptiform discharges occurring between seizures[35]. It has been reported that seizure frequency and the presence of EEG discharges may impair cognitive function and attention in patients with benign epilepsy with centrotemporal spikes[36]. Although associations between ADHD and EEG abnormalities have been reported in the literature, especially in children, no significant association was found between EEG findings and ADHD symptom levels in adult PWE in the present study. One possible reason for this is that the neurophysiological mechanisms underlying ADHD symptoms may not be directly visible in standard interictal EEG recordings[37].

In the present study, no significant association was found between ADHD symptoms and active epileptic seizures in adults with epilepsy. The literature on this topic remains inconsistent, with conflicting results. For example, in a study conducted on children with epilepsy, those who experienced seizures at least once per week demonstrated significantly higher levels of hyperactivity than those whose seizures occurred less frequently[38]. In contrast, another study found no significant differences in seizure frequency among children with epilepsy across various ADHD subtypes (combined type, inattentive type, and non-ADHD), indicating that seizure frequency may not be a dependable predictor of ADHD symptoms in all populations[39]. These conflicting findings may indicate the developmental

and neurobiological differences between children and adults with epilepsy. In children, frequent seizures can disrupt the maturation of neural networks, particularly in the prefrontal cortex and basal ganglia, which are essential for executive functioning and behavior inhibition[40]. In contrast, adults may exhibit compensatory mechanisms resulting from long-term illness adaptation or may have a lower seizure burden due to effective treatment, reducing the direct behavioral impact[41].

The duration of epilepsy, whether longer or shorter than 10 years, is a time frame used to assess treatment response, determine refractory status, and evaluate response to treatments such as resective surgery and vagal nerve stimulation in refractory patients. Patients with seizures for more than 10 years tend to have a poorer response to treatment than those with a shorter disease duration[42]. In the present study, no significant association was found between disease duration (≥10 years vs. <10 years) and ADHD-related characteristics in PWE. One possible explanation for this finding is that disease duration alone may not be a sufficient indicator of neurodevelopmental impact in adulthood. In contrast, previous studies have highlighted the importance of early age at seizure onset as a more critical factor. For example, Kwong et al. identified a negative correlation between ADHD symptom severity and age at seizure onset in adolescents[43]. Similarly, Caggia et al. also reported that earlier seizure onset increased the risk of ADHD in the pediatric epilepsy population[44]. Given recent evidence showing that early-onset epilepsy contributes to poorer neurodevelopmental outcomes[45], these findings suggest that early-onset seizures may have a more disruptive effect on brain maturation than the duration of the disease.

Epilepsy is linked to lower quality of life, functioning, and employment[46]. In the present study, a significant difference was found between the educational level and occupational distribution of PWE and the control group. The lower level of education and employment rate in PWE in the present study may be due to the disability caused by epilepsy.

To the best of our knowledge, this is the first study investigating the relationship between ADHD and chronotype in adult PWE. The fact that the PWE in the present study were not receiving antiepileptic treatment prevented any potential effects of antiepileptic drugs on our results.

The present study has several limitations that should be considered when interpreting the findings. First, the single-center, cross-sectional design limits the generalizability of the results and prevents causal inferences between variables. Although power analysis indicated an adequate overall sample size for group comparisons, the distribution of chronotype groups was uneven, especially due to the small number of participants in the evening-type category. This imbalance is a significant methodological limitation, as the small evening-type sample reduces statistical power and increases the risk of sampling bias. Thus, while the observed differences in Turgay 3 scores reached statistical significance, they should be interpreted with caution.

Another limitation involves excluding individuals with depressive or anxiety disorders, which limits the applicability of the findings to the broader epilepsy population, where such comorbidities are common. Additionally, chronotype was assessed solely using the MEQ, a widely used but subjective tool. Although validated, the MEQ does not fully account for physiological circadian rhythms. Including objective measures, such as actigraphy or dim light melatonin onset, would have improved the validity of chronotype classification. Future studies should aim to integrate both subjective and objective chronobiological data assessments.

Similarly, ADHD symptoms were assessed solely through self-report using the Turgay scale. Although this tool is validated and widely used, relying on self-report can be problematic, especially since individuals with ADHD may underestimate or overestimate their symptoms due to limited self-awareness. The absence of clinician-rated or multi-informant assessments may therefore lead to response bias.

Although seizure types were classified and reported descriptively in the present study, no subgroup analyses were performed because of the uneven distribution of epilepsy subtypes. Thus, epilepsy was treated as a single diagnostic category in an analytical way. This method, although practical due to sample size limitations, restricts the ability to determine if the observed associations—such as those between chronotype and ADHD symptoms vary significantly across different epilepsy subtypes (e.g., focal vs. generalized). Future studies with larger and more balanced subtype-specific cohorts are required to examine these differences more thoroughly.

Finally, neuroimaging data were reported based on the presence or absence of epileptogenic lesions as described in routine clinical MRI reports, without further classification regarding lesion types or specific anatomical locations. While this binary classification aligns with the study's design, it might have restricted the ability to identify links between specific structural abnormalities and ADHD symptomatology. Future research should incorporate more detailed neuroimaging analyses, including lesion localization and characterization, to better elucidate potential structural correlates of ADHD in PWE.

In conclusion, adult PWE exhibited significantly higher ADHD symptom scores compared to HC and evening chronotype was found to be associated with increased ADHD-related symptoms within the PWE. A negative correlation between chronotype scores and ADHD symptoms further supports the role of circadian preference in attentional function regulation. These findings indicate that chronotype is an important factor in understanding ADHD symptoms among PWE and should be taken into account during clinical assessments and interventions. From a clinical perspective, the findings of this study highlight the potential usefulness of chronotype assessment in identifying adult PWE who may be at higher risk for ADHD symptoms. In particular, higher ADHD symptom levels in PWE with an evening chronotype may help clinicians identify this group at an early stage. Furthermore, chronotherapeutic interventions, such as behavioral sleep strategies aimed at shifting the circadian rhythm to earlier hours, morning light therapy, or evening melatonin supplementation, may be considered in the treatment planning for evening chronotype PWE and comorbid ADHD symptoms. Studying these relationships in larger sample groups and various types of epilepsy through objective measurements will help clarify the issue.

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