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The relationship between social phobia and cognitive impairment in idiopathic generalized epilepsy patients: a cross-sectional study

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ABSTRACT

Objectives: Epilepsy, a neurological disorder affecting approximately 65 million people worldwide, frequently presents with various comorbidities, including cognitive impairment. The factors contributing to cognitive impairment are complex and multifaceted. This study aimed to investigate the influence of social phobia on cognitive function in patients with idiopathic generalized tonic-clonic epilepsy.

Methods: This prospective study recruited 87 adult idiopathic generalized tonic-clonic epilepsy patients diagnosed according to the International League Against Epilepsy 2017 classification. Differential diagnosis involved electroencephalography, magnetic resonance imaging, and neurological examinations. All participants were assessed for cognitive impairment, social phobia, depression, and anxiety using the Montreal Cognitive Assessment, Liebowitz Social Anxiety Scale, Beck Depression Inventory, and Beck Anxiety Inventory, respectively .

Results: A significant majority (73.6%) of participants reported social phobia. Compared to those without social phobia, the Montreal Cognitive Assessment total score was significantly lower in the social phobia group (P=0.002). Additionally, epilepsy duration was significantly longer in the social phobia group (P=0.03). Montreal Cognitive Assessment scores showed a negative correlation with Liebowitz Social Anxiety Scale-avoidance, Liebowitz Social Anxiety Scale-total, and age (P=0.003, P=0.005, and P<0.001, respectively).

Conclusion: This study suggests that individuals with idiopathic generalized tonic-clonic epilepsy experiencing social phobia may exhibit lower cognitive function compared to those without. This indicates that comorbid social phobia might negatively impact cognitive abilities in idiopathic generalized tonic-clonic epilepsy patients.

Keywords: Idiopathic generalized tonic-clonic epilepsy, social phobia, cognitive impairment, anxiety, depression

Epilepsy is a chronic neurological disease characterized by at least two unprovoked seizures occurring >24 hours apart and is a significant public health problem affecting 65 million people worldwide. The prevalence of active epilepsy ranges from 4 to 10 per 1000. The lifetime prevalence of epilepsy is 10.3 per 1000 in developing countries and 5.82 per 1000 in developed countries [1]. Epilepsy pa-

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tients often experience difficulties in their social and professional lives. Studies indicate that psychiatric comorbidities are common in these patients, reported at a rate of 19-71%. Comorbidities in epilepsy patients can sometimes be more burdensome than seizures, and the most common psychiatric comorbidities in epilepsy patients are mood disorders (24-74%), followed by anxiety disorders (10-25%), psychosis (2-7%) and personality disorders (1-2%) [2].

Social phobia, a marked fear or anxiety about one or more social situations in which an individual is subject to possible scrutiny by others, is a common disorder among anxiety disorders. Only a few studies evaluated social phobia in epilepsy patients [3, 4]. Moreover, social phobia is associated with an increased risk of cognitive impairment [5-7]. Cognitive impairment is a decline in cognitive abilities, such as memory, attention, and problem-solving that interferes with daily life. Cognitive impairment is a common problem in people with idiopathic generalized tonic-clonic seizures [8]. The severity of cognitive decline can vary from person to person. Studies have shown that up to 70% of people with generalized tonic-clonic seizures have some degree of cognitive impairment [8, 9].

There are only a limited number of studies exploring the connection between social phobia and generalized tonic-clonic seizures [6, 7]. Furthermore, to our knowledge, no research has yet examined the relationship between social phobia and cognitive impairment in this specific patient population. This study was designed to primarily investigate the connection between cognitive impairment and social phobia, depression, and anxiety in individuals with generalized tonic-clonic seizures. Additionally, we aimed to analyze the potential associations between cognitive impairment and factors such as age, gender, epilepsy duration, seizure frequency, and medication use.

METHODS

Study Overview

This prospective study, carried out between March and July 2023 in a neurology outpatient clinic of a tertiary hospital. Informed written consent was obtained from all patients.

Ethical Considerations

This study was approved by the Kastamonu University Ethics Committee (project number 2023-KAEK-22).

Study Population

The study included 87 adult epilepsy patients diagnosed with idiopathic generalized tonic-clonic epilepsy, according to The International League Against Epilepsy 2017 (ILAE), who applied to the Neurology Outpatient Clinic of a tertiary hospital. Patients diagnosed with a psychiatric disease or intellectual disability (n=14), those with neurological disease other than epilepsy (n=7), patients under the age of 18 (n=3), those with any severe and progressive organic disease (n=1), those with any structural lesion in the brain identified using magnetic resonance imaging (MRI) (n=5), those who had seizures in the last one month (n=9), patients with seizures other than generalized tonic-clonic seizures (JTKSs) (n=11), and patients over 65 years of age (n=9) were not included in the study. A neurologist examined all 87 patients (18-61 years) with epilepsy.

Study Procedure

The patients were asked questions about their age, gender, education level, personal and familial medical history, duration of epilepsy, age of onset of epilepsy, frequency of seizures, and drug use. Differential diagnosis was made using electroencephalography (EEG), MRI, and neurological examination. Seizure frequencies in the last month were recorded. Who received one of the first, second or third generation anti-seizure drugs were grouped as monotherapy and who received them together were grouped as polytherapy. Montreal Cognitive Assessment (MoCA) was applied to test the cognitive status of the patients, Liebowitz Social Phobia Scale (LSPS) was applied to detect the presence and degree of social phobia, and Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were applied to determine depression and anxiety states, respectively.

Study Assessment

MoCA: This assessment comprises 11 sections, including tracing tests, visual construction skills (cube and clock), naming, memory, attention, sentence repetition, verbal fluency, abstract thinking, delayed recall, and orientation. The maximum achievable score

on the test is 30. A total score of 21 and above is considered within normal limits [9]. Kaya *et al*. [10] conducted a validity and reliability study of the test in Turkish society.

LSPS: This instrument consists of two parts. The first part comprises 24 questions scored between 0 and 3 based on the severity of anxiety experienced in described situations. The second part consists of 48 questions, with 24 questions scored between 0 and 3 based on the severity of avoidance in the same situations. While the validity and reliability study did not specify a cut-off value, some studies suggested a cut-off value of 30 [11, 12]. In this study, the LSPS total score was used in statistical analysis, and groups were created as having or not having social phobia using the LSPS cut-off score.

BDI: This scale comprises a total of 21 questions, asking the patient to reflect on their condition in the last week [13]. In the validity and reliability study conducted on the Turkish population by Kapci *et al*. [14], scores of 0-9 indicate minimal depression, 10-16 indicate mild depression, 17-29 indicate moderate depression, and 30-63 indicate severe depression.

BAI: This scale consists of 21 questions with four options, asking the participant to consider the last week [15]. Ulusoy *et al*. [16] conducted a validity and reliability study in the Turkish population, where scores of 8-15 indicate mild anxiety, 1625 indicate moderate anxiety, and 26-63 indicate severe anxiety.

Sample Size Estimation

Using G*Power version 3.1.9.4 for sample size estimation, A prior power analysis was performed based on published study data; The effect size (correlation pH1) in the published study, in which cognitive functions in epilepsy patients were evaluated by MoCA score and correlation analysis with 70 participants [6], was 0.335. Significance criterion=α. 05 and power=.80, the minimum sample size required for a medium effect size is N=84 [for correlation analysis]. Therefore, the resulting sample size N=84 is sufficient to test the study hypothesis.

Statistical Analysis

Data analysis was conducted using SPSS for Windows version 21.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was employed to assess the normality of the data distribution. Descriptive statistics

Table 1. Sociodemographic and clinical characteristics of epilepsy patients

Variable	Data
Age (years)	34.06±11.86
Education (years)	9.01±3.07
Disease duration (years)	12.99±10.47
Number of seizures in the last year	2.73±3.75
Gender, n (%)	
Male	38 (43.7)
Female	49 (56.3)
Marital status, n (%)	
Single	42 (48.3)
Married	45 (51.7)
Place of residence, n (%)	
Rural	24 (27.6)
Urban	63 (72.4)
Smoking, n (%)	
Yes	14 (16.1)
No	73 (83.9)
Alcohol use, n (%)	
Yes	4 (4.6)
No	83 (95.4)
Anti-seizure use, n (%)	
Monotherapy	63 (72.4)
Polytherapy	24 (27.6)
MoCA (cut-off score 21) Cognitive impairment, n (%)	
Yes	40 (46)
No	47 (54)
LSPS (cut-off score 30) Social phobia, n (%)	
Yes	64 (73.6)
No	23 (26.4)
BAI (cut-off point 16) Anxiety, n (%)	
None or mild	59 (67.8)
Moderate or severe	28 (32.2)
BDI (cut-off point 17) Depression, n (%)	
None or mild	63 (72.4)
Moderate or severe	24 (27.6)

Data are shown as mean±standard deviation or n (%). MoCA=Montreal Cognitive Assessment Scale, LSPS=Liebowitz Social Phobia Scale, BDI=Beck Depression Inventory, BAI=Beck Anxiety Inventory,

presented the data, with frequencies and percentages for categorical variables. Continuous variables with normal distributions were expressed as mean±standard deviation, while those without normal distributions were presented as median (maximum-minimum).

For comparisons between numerical values, the Mann-Whitney U test was applied. Categorical values were compared using the Chi-square test. Correlation analysis involved Pearson's correlation coefficient for normally distributed values and Spearman's correlation coefficient for non-normally distributed values. A P-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 38 (43.7%) participants were male, 49 (56.3%) were female, 42 (48.3%) were single, and 45 (51.7%) were married. The mean age of the participants was 34.06±11.86 years, and the duration of education was 9.01±3.07 years. Of the 87 patients, 24 (27.6%) lived in rural areas, while 63 (72.4) lived in urban areas. The disease duration of epilepsy patients was 12.99±10.47 years, the number of seizures in the last year was 2.73±3.75, 63 (72.4%) individuals were receiving monotherapy, and 24 (27.6%) were receiving polytherapy as anti-seizure treatment. In the evaluation with the MoCA scale, cognitive impairment was detected in 40 (46%) participants. When evaluated according to the cut-off values of the scales (LSPS, BAI, BDI) 64 (73.6%) individuals had social phobia, 28 (32.2%) had significant anxiety and 24 (27.6%) had significant depressive symptoms (Table 1).

No significant differences were identified between the groups with and without social phobia concerning age, education, gender, and the number of seizures in the last year (P>0.05). However, it was observed that the group with social phobia had a significantly lower MoCA total score and a significantly longer disease duration compared to the group without social phobia (P=0.002 and P=0.030, respectively). When comparing groups receiving monotherapy and polytherapy, no significant differences were found in terms of age,

Table 2. Comparison of the group with and without social phobia

Variable	No Social Phobia Group	Social Phobia Group	P value
Age	30.78±13.74	35.23±10.99	**0.052****
Education (years)	12.00 (5.00-12.00)	8.00 (5.00-14.00)	0.414**
Gender, number (%)			0.338*
Male	12 (52.2)	26 (40.6)	
Female	11 (47.8)	38 (59.4)	
MoCA total	24.22±3.86	20.55±4.82	**0.002****
Disease duration (year)	5.50 (1.00-33.00)	10.50 (1.00-44.00)	**0.030****
Last year's seizure	0.00 (0.00-12.00)	1.50 (0.00-12.00)	0.260**
	Monotherapy group	**Polytherapy group**	
Age, mean ± SD	34.90±12.11	31.83±11.10	0.300**
Education (years)	8.00 (5.00-14.00)	8.00 (5.00-12.00)	0.503**
Gender, number (%)			0.473*
Male	29 (46)	9 (37.5)	
Female	34 (54)	15 (62.5)	
MoCA total	20.95±5.10	23.00±3.82	0.098**
Disease duration	9.00 (1.00-44.00)	18.50 (1.00-35.00)	0.240**
Last year's seizure	1.00 (0.00-12.00)	2.00 (0.00-12.00)	0.400**

Data are shown as mean±standard deviation or median (minimum-maximum or n (%). MoCA=Montreal Cognitive Assessment Scale, *Chi-square test, **Mann Whitney U test

Table 3. Comparison of MoCA total score with clinical features

	MoCA Total	
	R	P value
Age	−0.449	**<0.001***
Education	0.458	**<0.001****
Disease duration	−0.144	0.182**
Last year seizure	−0.033	0.763**
LSPS-avoidance	−0.317	**0.003***
LSPS-anxiety	−0.168	0.120**
LSPS-total	−0.296	**0.005****
BDI	0.005	0.966**
BAI	−0.154	0.154**

MoCA=Montreal Cognitive Assessment Scale, LSPS=Liebowitz Social Phobia Scale, BDI=Beck Depression Inventory, BAI=Beck Anxiety Inventory, *Pearson correlation analysis, **Spearman correlation analysis

education, gender, MoCA total score, disease duration, and the number of seizures in the last year (P>0.05) (Table 2).

When the relationship between the MoCA total score and the variables was evaluated, the MoCA total score was weakly negatively significant (r= −0.317, P=0.003; r= −0.296, P=0.005) with the LSPS-avoidance and LSPS-total scores and moderately negatively significant (r =−0.449, P<0.001) with age while there was a moderately positive significant (r=0.458, P<0.001) relationship with education (Table 3).

DISCUSSION

In our study, a substantial proportion of epilepsy patients (73.6%) exhibited social phobia. When comparing individuals with and without social phobia, no statistically significant differences were observed in age, education level, gender, or seizure frequency in the last year. However, the group with social phobia had a significantly lower MoCA total score compared to the group without social phobia. Additionally, a negative significant relationship was observed between the MoCA total score, LSPS-avoidance, and LSPS-total scores, as well as age. Conversely, there was a positive and meaningful relationship with education.

Cognitive impairment is a common complication of epilepsy, affecting up to 50% of patients, and is a result of various factors such as the patient's age, seizure frequency, and polytherapy [5]. The relationship between seizure frequency and cognitive decline in epilepsy is complex. Some studies have found a correlation between seizure frequency and cognitive decline, while others have not. Voltzenlogel *et al*. [17] found a correlation between seizure frequency and cognitive decline in refractory epilepsy patients. Black *et al*. [18] found that frequent seizures caused a significant decrease in cognitive functions in patients with temporal lobe epilepsy. In their research, Taylor *et al*. [19] identified seizure frequency as a crucial factor influencing cognitive abilities in untreated epileptic patients [19]. However, Piazzini *et al*. [20] found no correlation between seizure frequency and cognitive impairment in epilepsy patients. Our study found cognitive impairment in 46% of epilepsy patients, similar to the literature. However, we found no significant relationship between seizure frequency and cognitive decline. This result may be due to the low number of patients with frequent seizures in our cohort or to the fact that we exclude patients with brain structural lesions that may cause cognitive impairment [21].

Cognitive impairment is common in epilepsy patients receiving high-dose and multiple anti-seizure treatments [22]. It is primarily manifested in executive functions [23]. Most anti-seizure drugs (ASDs) have mental side effects such as inattention, insomnia, and dizziness [24]. The relationship between cognitive impairment and medication in epilepsy is complex. Some studies have found that polytherapy is associated with worse cognitive function, but others have not [24]. The higher incidence of cognitive impairment in patients receiving polytherapy may be due to resistant and frequent seizures [24]. Interestingly, our study found no significant difference in cognitive impairment between groups taking polytherapy and those on monotherapy. This could potentially be due to the younger average age of the polytherapy group.

Anxiety is a common comorbidity in epilepsy patients, with a reported prevalence of around 20% [25]. However, the relationship between anxiety and cogni-

tive function in epilepsy patients is complex and poorly understood. Some studies have found an association between anxiety and cognitive impairment. For example, Miller *et al*. [26] found that higher anxiety levels were associated with worse visual memory outcomes in epilepsy patients. Velissaris *et al*. [27] found that epilepsy patients with high anxiety levels had lower cognitive function scores. Our study found that anxiety levels were high (32.2%), but there was no significant relationship between anxiety and cognitive impairment.

Depression is a common comorbidity in epilepsy patients, with a reported prevalence of around 20-30% [28-32]. It has been associated with many factors, including seizure frequency, type of epilepsy, medication use, and occupational activity [23]. Our study revealed a prevalence of moderate-to-severe depression in 27.6% of epilepsy patients, consistent with the literature. However, we did not find a statistically significant link between depression symptoms and cognitive impairment.

The number of studies investigating social phobia in epilepsy patients is limited [3,4]. Moreover, to the best of our knowledge, no prior study has explored the specific interaction between social phobia and cognitive function in epilepsy patients. Kutlu *et al*. [4] showed that patients with epilepsy had significant levels of social phobia compared to healthy control groups. In a recent study, especially persistent seizures were related to social phobia in males [33]. A study conducted in China showed that social anxiety is independently associated with low quality of life [34]. In our study, social phobia symtoms were observed in 73.6% of the patients. Notably, individuals in the social phobia group demonstrated significantly lower overall scores on the MoCA compared to those without social phobia. This suggests a potential link between social anxiety and cognitive impairment in epilepsy patients. The underlying mechanisms responsible for the association between social phobia and cognitive impairment remain unclear. However, social phobia may lead to social isolation, a known risk factor for cognitive decline. Furthermore, social phobia may be associated with underlying cognitive deficits that hinder engagement in social activities. For instance, individuals with social phobia may experience difficulties with memory, attention, and executive functioning. These cognitive impairments can make it challenging to maintain social connections and engage in stimulating activities, further contributing to cognitive decline [7, 8].

Limitations

This study has some limitations. Considering the sample size was not very large, groups could not be formed according to individual drug use, and scale scores could not be compared. Our study is a cross-sectional measurement, and the type of data collection tools we used may be reflected in our findings; longitudinal studies are needed for more valid evidence. The patients' levels of anxiety, depression, and social phobia were measured using the BAI, BDI, and LSPS scales, respectively. The patients were unable to have a comprehensive psychological examination.

CONCLUSION

The group with social phobia exhibited a significantly lower MoCA total score, and the duration of the disease was significantly longer compared to the group without social phobia. In conclusion, the presence of comorbid social phobia in epilepsy patients appears to be linked to poorer cognitive functions. Offering social and psychological support to these patients regarding social phobia may prove beneficial in preserving cognitive functions.

Authors' Contribution

Study Conception: İK, Aİ; Study Design: İK, Aİ; Supervision: İK, Aİ; Funding: İK, Aİ; Materials: İK, Aİ; Data Collection and/or Processing: İK, Aİ; Statistical Analysis and/or Data Interpretation: İK; Literature Review: İK; Manuscript Preparation: İK, Aİ and Critical Review: İK, Aİ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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