Social Anxiety Level in Adult Patients With Epilepsy and Their First-Degree Cohabiting Relatives

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Epilepsy affects not only the patient but also the patient's cohabiting relatives, to various degrees. This study investigated state and trait anxiety, depression, and social fear and avoidance levels in 48 adult patients with epilepsy and 48 family members, compared with 43 healthy control subjects, using the Beck Anxiety Inventory, the Beck Depression Inventory, the State-Trait Anxiety Inventory, and the Liebowitz Social Anxiety Scale. The results suggested that the patients and their first-degree relatives had higher levels of depression, state and trait anxiety, and avoidance compared with healthy subjects. The mothers of patients with epilepsy had the highest level of depression and anxiety.

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Epilepsy is a chronic neurological disease characterized by recurrent, unprovoked seizures. Epilepsy ranks as the second most common complaint in neurology clinics, after headaches. The prevalence of active epilepsy varies between 4 and 10 per 1,000. Although the prevalence of lifelong epilepsy is 5.8 per 1,000 in developed countries, it is 10.3 per 1,000 in urban populations of developing countries.[1]

Patients may frequently experience impairment in quality of life and in social, vocational, and family relationships, and psychiatric comorbidities may appear over the course of epilepsy. Epidemiological studies reported psychiatric comorbidities at a rate of 19%−71% in patients with epilepsy.[2–4] The most prevalent psychiatric comorbidities in epilepsy are mood disorders (24%−74%), with depression constituting 30% of these disorders, followed by anxiety disorders (10%−25%), psychosis (2%−7%), and personality disorders (1%−2%).[5]

Epilepsy affects not only the patient but also the patient's cohabiting relatives, to various degrees. Families of children who are diagnosed with epilepsy report having high stress, and mothers of patients with epilepsy report depression and impaired family functions at a high rate.[6,7] Past research demonstrated high levels of anxiety in parents of children with uncontrolled seizures and comorbid disability that causes inadequacy; in addition, the mothers of these children have a high rate of state anxiety. This leads to impairment in family relationships and lifestyle.[8–10] However, to our knowledge, there are no similar studies conducted with adult patients.

Diagnosing and treating social anxiety disorders is important because these disorders may result in social disability, loss of self-respect, phobic avoidance, impaired lifestyle, fear of experiencing a seizure in public, and social stigmatization. In this study, our goal was to determine the respondents' level of state and trait anxiety and social anxiety by using the Liebowitz Social Anxiety Scale with adult patients with epilepsy and their cohabiting relatives (e.g., mother, father, spouse, sister, or brother). We also examined whether epileptic seizures affected the social lives of patients and their cohabitants.

METHODS

Participants

This prospective study, which was carried out from June to December 2013, was approved by the Baskent University Institutional Review Board (project number KA 13/114) and was supported by the Baskent University Research Fund. The study included 48 adult patients with epilepsy who were admitted to the neurology clinic of Baskent University, their 48 cohabiting relatives, as well as 43 healthy control subjects.

All of the patients gave written informed consent. Parents signed the consent form for patients <18 years old. Exclusion criteria included schizophrenia, schizophreniform disorder, bipolar affective disorder, mental retardation, other neurological disorders, age <15 years, a history of any serious and progressive organic disease, and, for women, being pregnant or breastfeeding.

All 48 patients with epilepsy (15–56 years old) were examined by a neurologist. The patients responded to questions about their age, gender, educational level, personal and

family medical history, duration of epilepsy, age at the onset of epilepsy, frequency of seizures, and drug usage. The differential diagnosis was made via EEG, MRI, and neurological examination. The frequency of seizures was classified as very frequent (every day to 7 days), frequent (7–30 days), rare (31 days to 1 year), or very rare (<1 per year). The types of epileptic seizures were categorized as follows: primary generalized epilepsy (generalized tonic-clonic, myoclonic and absence) and focal epilepsy (focal motor seizures, complex partial and secondary generalized).

After the neurological evaluation, a psychiatrist examined the patients and questioned them about their social support and feelings about the disease. The psychiatrist also evaluated any of the patients' stressful life events experienced over the past 6 months in detail via semistructured interviews. Stressful life events included business, education, finance, health, grief, and migration, and legal, familial, social, and marital problems. Psychiatric comorbidities were diagnosed using the Structured Clinical Interview for DSM-IV. We explained the self-report measures to the patients before they completed the questionnaires.

Measures

In this study, the Beck Anxiety Inventory, the Beck Depression Inventory, the State-Trait Anxiety Inventory (STAI)-I, and the STAI-II were completed by the patients, their cohabiting relatives, and the control group. The Liebowitz Social Anxiety Scale was completed by an interviewer.

The Turkish version of the Beck Depression Inventory was used to assess the prevalence and severity of depressive symptoms.[11] The Beck Depression Inventory is a self-report inventory created by Aaron Beck; it consists of 21 items that respondents rank from 0 to 3. The total possible score ranges from 0 to 63. A score of 0–13 indicates none/minimal depression, whereas scores of 14–19, 20–28, and 29–63 indicate mild, moderate, and severe depression, respectively. Individuals with a Beck Depression Inventory score ≥14 are usually categorized as depressed. A reliability and validity study of the Turkish version of the Beck Depression Inventory suggested that a score ≥17 should be used as an indicator of major depression in the Turkish population.[12]

The Beck Anxiety Inventory is a 21-item scale that is widely used to measure the severity of anxiety.[13] Acceptable validity and reliability have been reported in various populations. We used the Turkish version of the Beck Anxiety Inventory, which is validated for use in the Turkish population.[14] Like the original Beck Anxiety Inventory, in the Turkish version, each item is scored from 0 to 3, with 3 representing the most severe anxiety. A total score of 0–7 is interpreted as none/minimal level of anxiety, whereas scores of 8–15, 16–25, and 26–63 are interpreted as mild, moderate, and severe anxiety, respectively. The scores for each of these 21 items were summed at the end of the psychological evaluation.

The STAI-I and STAT-II are paper-and-pencil questionnaires that can be performed with individuals ≥14 years old who can understand what they read.[15] The STAI-I determines how anxious a person feels at a certain time or under certain conditions, whereas the STAI-II targets how a person generally feels, independent of the patient's current condition. We used a validated and reliable Turkish version of the inventory.[16,17] A total score obtained from each scale varies between 20 and 80. During the comparison, the highest score indicates the highest level of anxiety.

The Liebowitz Social Anxiety Scale was developed by Liebowitz in 1983. The measure is administered by the interviewer to determine levels of fear/anxiety and avoidance in the patient with social anxiety disorder in social interplay and performance conditions. The measure comprises 24 items, including 13 performance scenarios and 11 social interplay scenarios. The original and Turkish versions of the scale are valid and reliable, and a cutoff score is not discounted in the Turkish version.[18,19] In this study, total scores for each fear/anxiety and avoidance scenario are compared statistically.

Sample Size Estimation

The Win Epi 2.0 program was used for sample size estimation. Our calculations indicated that 30 subjects for each group would allow 95% confidence intervals and 80% power.

Statistical Methods

SPSS 17.0 software (SPSS Inc., Chicago, IL) was used for the statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, whereas continuous measurements were summarized as means and standard deviations (or medians and minimums to maximums where necessary). Chi-square or Fisher test statistics were used to compare categorical variables. For the comparison of continuous measurements between groups, distributions were controlled for normality according to the number of variables. One-way analysis of variance was used for the parameters that showed a normal distribution, and the Kruskal-Wallis test was used for parameters that did not show a normal distribution. Post hoc analyses were planned for significant results. The Kolmogorov-Smirnov test was used for checking normality of the data distribution. For all analyses, the level of statistical significance was $p<0.05$.

RESULTS

Sociodemographic Variables

The study comprised 139 subjects, including 48 patients with epilepsy, 48 first-degree relatives, and 43 healthy control subjects. The mean age was 27.46±9.28 years (range, 15–56 years) for the patients with epilepsy, 39.48±9.87 years (range, 20–70 years) for their cohabiting relatives, and 38.28±10.9 years (range, 19–65 years) for healthy control subjects. There was a statistically significant difference between the patients and controls as well as between the patients and relatives in terms of age. The age of the relatives

and controls was similar. The three groups were similar in terms of gender distribution.

Twenty-three of the relatives surveyed were the parents of the patient. Aside from these relatives, three others were brothers or sisters of the patients and 22 were partners of the patients. Marital status and educational level were significantly different among patients, relatives, and control subjects. Consanguinity was present in 14 patients (29.2%). Sociodemographic characteristics of all groups (univariate analyses) are shown in Table 1.

TABLE 1. Comparison of the Groups by Sociodemographic Characteristics[a]

Characteristic	Group 1	Group 2	Group 3	Total	p Value
Gender					0.89
Male	17 (35.4)	18 (37.5)	14 (32.6)	49 (35.3)	
Female	31 (64.6)	30 (62.5)	29 (67.4)	90 (64.7)	
Education, years					0.00
≤8	14 (29.2)	31 (64.6)	9 (20.9)	54 (38.8)	
9–11	17 (35.4)	8 (16.7)	18 (41.9)	43 (30.9)	
>11	17 (35.4)	9 (18.8)	16 (37.2)	42 (30.2)	
Employment status					0.00
Housewife	17 (35.4)	25 (52.1)	10 (23.3)	52 (37.4)	
Employed	10 (20.8)	14 (29.2)	18 (41.9)	42 (30.2)	
Retired	2 (4.2)	3 (6.3)	4 (9.3)	9 (6.5)	
Student	17 (35.4)	0 (0.0)	4 (9.3)	21 (15.1)	
Clerical	2 (4.2)	6 (12.5)	7 (16.3)	15 (10.8)	
Marital status					0.00
Single	25 (52.1)	2 (4.2)	6 (14.0)	33 (23.7)	
Married	23 (47.9)	46 (95.8)	35 (81.4)	104 (74.8)	
Divorced	0 (0.0)	0 (0.0)	2 (4.7)	2 (1.4)	
Cigarette use					0.00
Smoker	8 (16.7)	0 (0.0)	0 (0.0)	8 (5.8)	
Nonsmoker	40 (83.3)	48 (100.0)	43 (100.0)	131 (94.2)	
Trauma history	18 (37.5)	0 (0.0)	0 (0.0)	18 (12.9)	0.00

[a] Data are presented as N (%).The chi-square test was used to compare categorical variables. The Kruskal-Wallis test was used to calculate p values. Group 1 comprises patients with epilepsy, group 2 includes first-degree relatives of patients with epilepsy, and group 3 comprises healthy control subjects.

Clinical Characteristics

Epileptic findings. The neurological examination revealed normal findings in 42 patients. By contrast, two patients had postural tremors in their hands, and one patient had decreased hearing. In addition, one patient had mild left hemiparesis, and another had bilateral hip dysplasia. One patient had natal sequela in the left arm.

MRI revealed normal findings in 40 patients. The pathological findings on MRI included right mesial temporal sclerosis, bilateral mesial temporal sclerosis, hydrocephalus, right frontotemporal encephalomalacia, right temporoparietal encephalomalacia, right temporal encephalitis, bilateral cerebral cortical tubers, and right frontal cortical dysplasia, each of which was found in one unique patient.

EEG demonstrated normal findings in 15 patients, whereas 20 patients had diffuse epileptic discharges, nine patients had epileptic activity in the right hemispheric areas, and four patients had epileptic activity in the left hemispheric areas.

The mean age at the onset of epilepsy was 17.15 years (range, 1–54 years), and the mean examination age was 26.6 years (range, 1–55 years). Of the patients with epilepsy, 60.4% had focal epilepsy and 39.6% had primary generalized epilepsy. Patients reported the following seizure frequencies: very frequent, 12.8% (every day to 7 days); frequent, 10.6% (7–30 days); rare, 36.2% (31 days to 1 year); and very rare, 40.4% (<1 per year).

Although 97.9% of the patients were receiving epileptic drug therapy (e.g., valproic acid, 35.4%; levetiracetam, 22.9%; carbamazepine, 45.8%; lamotrigine, 10.4%; and topiramate, 8.3%), one of the patients was not receiving any drug therapy. The ratio of patients taking two antiepileptic drugs in combination was 20.8%, whereas the ratio of patients taking three antiepileptic drugs in combination was 2.1%. The remaining patients (77.1%) were taking only one antiepileptic drug (Table 2).

The duration of disease in patients with epilepsy was <1 year in 17%, 1–3 years in 14.9%, and >3 years in 68.1%. There was a significant correlation between the duration of epilepsy and scores on the STAI-I, the STAI-II, and the Beck Depression Inventory ($p<0.05$). The patient who had the longest duration of disease had the highest scores. However, there was no significant relationship between the type of epileptic seizure and the scores on the psychiatric scales (Table 3).

Psychiatric findings. How patients described the disease was categorized as follows: disease (70.8%), mental disorder (2.1%), a burden for the family (41.6%), anxiety/worthlessness (14.6%), and all of the above (6.2%). How patients felt about themselves was categorized as follows: abnormal (4.2%), different (31.2%), ill (25%), ashamed (10.4%), worried (35.4%), a danger to oneself (22.9%), and a danger to others (35.4%). Of the patients, 60.4% had experienced stressful life events in the last 6 months, and 97.9% reported having social support (Table 2).

All three groups showed statistically significant differences in their scores on the STAI-II, the Beck Anxiety Inventory, the Beck Depression Inventory, and the Liebowitz Social Anxiety Scale fear/anxiety and avoidance subscales. Paired comparisons between the patients and their relatives revealed no differences in the scores. However, paired comparisons between patients and controls and between relatives and controls demonstrated statistical differences in scores on all of the scales (Table 4).

The mothers of patients with epilepsy had the highest scores on most of the scales. However, the Liebowitz Social Anxiety Scale fear/anxiety and avoidance subscale scores were similar in sisters/brothers and mothers. In addition,

TABLE 2. Clinical Features of Patients With Epilepsy[a]

Characteristic	Value
Epilepsy onset age in years	48 (17.1±11.5)
Examination age in years	48 (26.6±9.6)
Consanguinity between mother and father	14 (29.2)
Stressful life events	29 (60.4)
Social support	47 (97.9)
Seizure frequency	
Very frequent (every day out of 7 days)	6 (12.8)
Frequent (7 of 30 days)	5 (10.6)
Rare (31 days out of 1 year)	17 (36.2)
Very rare (less than once per year)	19 (40.4)
Epileptic seizure type	
Primary generalized epilepsy	19 (39.6)
Focal epilepsy	29 (60.4)
Epileptic drug type	
Not taking any drug	1 (2.1)
Valproic acid	17 (35.4)
Levetiracetam	11 (22.9)
Carbamazepine	22 (45.8)
Lamotrigine	5 (10.4)
Topiramate	4 (8.3)
How would you describe epilepsy?	
Disease	34 (70.8)
Mental disorder	1 (2.1)
Burden for the family	20 (41.6)
Worthlessness	7 (14.6)
All of the above	3 (6.2)
How do the seizures make you feel?	
Abnormal	2 (4.2)
Different	15 (31.2)
Sick	12 (25.0)
Ashamed	5 (10.4)
Worried	17 (35.4)
Insecure to himself/herself	11 (22.9)
Insecure to others	17 (35.4)
None	7 (14.6)

[a] Data are presented the mean ± standard deviation or N (%). The chi-square test was used to compare categorical variables.

scores on the scales were mostly similar in the partners and fathers (Table 5).

DISCUSSION

To our knowledge, this study is the first that compares social anxiety and state and trait anxiety among adult patients with epilepsy and their first-degree relatives. Our study suggested that patients and their first-degree relatives had higher levels of depression, state and trait anxiety, and avoidance compared with healthy control subjects. Second, our results suggested that the types of epileptic seizures were not associated with the level of anxiety or depression in our patients or in their relatives. Third, we found that the mothers of patients with epilepsy had the highest level of depression and anxiety.

Depressive disorder, together with anxiety disorder, is the most common psychiatric comorbidity in patients with epilepsy.[5,20–22] Studies have reported that the prevalence of anxiety disorders is 14.8%−25% in patients with epilepsy.[23–25] Other psychiatric comorbidities and their prevalence rates are as follows: generalized anxiety disorder (3%−12%), panic disorder (5%−21%), social anxiety disorder (3%−7%), post-traumatic stress disorder (1%), and obsessive-compulsive disorder (1%−5%).[25–27]

Epileptic seizures affect not only the patient but also all members of the patient's family. The available studies focused on assessing the level of depression and anxiety in children with epilepsy and in their mothers. These studies found depression and anxiety levels to be higher in mothers of children with epilepsy compared with mothers of healthy children.[8–10,28] We studied patients and their relatives who had different levels of consanguinity and found that mothers had the highest scores on most of the scales, as mentioned in the above study. Because of the absence of similar studies, we cannot compare all of our results with existing studies in the literature. We performed this study because of a lack of similar studies in adult patients. We determined that social anxiety, depression, and state and trait anxiety levels were higher in patients with epilepsy and in their family members compared with a control group of healthy individuals.

Various factors may play a role in the development of anxiety disorders and in the activity of neurotransmitter pathways in patients with epilepsy. These factors may include age at the onset of epilepsy, type of epilepsy (mostly focal and temporal lobe), frequency of seizures, interictal or ictal EEG disorders, side effects related to drugs used for treatment, surgery for treatment, psychiatric comorbidities, disease-related social and vocational problems and stigmatization, decrease in self-respect, extremely protective behavior from the family, and conditioning from experiences with unexpected seizures in the past.[5]

Fear and anxiety are the basic characteristics of anxiety disorders. The feeling of fear may be modulated by the frontal cortex and the orbitofrontal cortex, which are the key areas of the prefrontal cortex that regulate feelings and reciprocal circuits shared by the amygdala. The cortico-striatal-thalamic-cortical cycle may play an important role in the response to anxiety. Moreover, GABA-A, norepinephrine, serotonin, and dopamine neurotransmitters also play a role in both epilepsy and anxiety disorders.[29–31]

TABLE 3. Comparisons of Scale Scores Between Seizure Types[a]

Scale	Generalized Epilepsy	Focal Epilepsy	Total	p Value
LSAS				
Anxiety subscale	51 (26–77)	53 (26–812)	51 (26–81)	0.94
Avoidance subscale	51 (26–84)	51 (26–80)	51 (26–84)	0.95
BAI	19 (5–45)	18 (1–44)	18 (1–45)	0.75
BDI	11 (4–27)	14.5 (3–35)	13 (3–35)	0.14
STAI-I	39 (25–55)	46 (21–76)	41 (21–76)	0.24
STAI-II	49 (35–56)	49 (23–71)	49 (23–71)	0.63

[a] Data are presented as the median (minimum–maximum). The Kruskal-Wallis test was used to calculate p values. BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; LSAS, Liebowitz Social Anxiety Scale; STAI, State-Trait Anxiety Inventory.

TABLE 4. Comparisons of the Scale Scores Among Groups[a]

Scale	Group 1	Group 2	Group 3	Total	p Value	p Values for Group Comparisons		
						Groups 1 and 2	Groups 1 and 3	Groups 2 and 3
BAI	18.5 (1–45)	14 (1–41)	7 (1–45)	13 (1–45)	0.00	0.14	0.00	0.00
BDI	13 (3–35)	12 (2–43)	7 (2–26)	11 (2–43)	0.00	0.55	0.00	0.002
STAI-I	41.5 (21–76)	37 (20–70)	33 (22–57)	37 (20–75)	0.00	0.84	0.05	0.09
STAI-II	49.5 (23–71)	44 (27–72)	39 (30–58)	44 (23–72)	0.00	0.34	0.00	0.002
LSAS								
Anxiety subscale	51.5 (26–81)	48.5 (24–73)	34 (25–46)	41 (24–81)	0.11	0.48	0.00	0.00
Avoidance subscale	51.5 (26–84)	50.5 (24–76)	35 (24–46)	43 (24–84)	0.00	0.62	0.00	0.00

[a] Data are presented as the median (minimum–maximum). The Kruskal-Wallis test was used to calculate p values, except for the group comparisons, which were calculated with the post hoc Mann-Whitney U test ($p \leq 0.02$, Bonferroni correction). Group 1 comprises patients with epilepsy, group 2 includes first-degree relatives of patients with epilepsy, and group 3 comprises healthy control subjects. BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; LSAS, Liebowitz Social Anxiety Scale; STAI, State-Trait Anxiety Inventory.

Social anxiety disorder is defined as the fear of social conditions that involve interaction with other people, fear of being insulted, or fear of feeling ashamed or foolish. According to *DSM-IV*, the individual feels fear of showing prominent anxiety signs and physiological signs of anxiety. These signs may be limited to a few occasions, such as eating, writing, or making speeches in public, or they may be common, occurring in many social situations.[18] Generally, social anxiety disorder appears between the ages of 13 and 24 years in single women and may cause serious disturbances in vocational, social, and academic performance. Psychodynamic, conditioned, and cognitive models, as well as personality disorders and genetic and biological factors, play a role in the etiology. In the available studies, the prevalence of social anxiety disorders in patients with epilepsy was 3%−7%.[25,26] In this study, we found that both anxiety/fear and avoidance subscale scores from the Liebowitz Social Anxiety Scale were higher in patients with epilepsy and their relatives, particularly in the patients' mothers.

Anxiety and focal epileptic seizures have similar underlying mechanisms. The amygdala and hippocampus play major roles in both disorders.[32] Among all types of epilepsy, temporal lobe epilepsy is most frequently associated with ictal fear.[33] Edeh and Toone[24] suggested that comorbid anxiety is higher in temporal lobe epilepsy and focal nontemporal lobe epilepsy, compared with generalized epilepsy. Smith et al.[34] found that how patients perceive seizures is a more important predictor of anxiety. In our study, we found that the type of epileptic seizure (general or focal) was not associated with the psychological well-being of patients or their first-degree relatives.

Our study had several limitations. For example, this study's cross-sectional design restricts our ability to make inferences about causation. In addition, because the sample was selected from a single center, our results may not be generalizable to the population. Measuring constructs using self-report scales may also be a limiting factor. In addition, analyzing parents, siblings, and partners together may also be a limitation to our study. Another possible limitation is that we obtained patients' history of epileptic seizures by reviewing retrospective reports from the patients or their families. We also did not evaluate stressful life events using a standardized scale. Finally, particular drugs may be associated with negative psychotropic effects, which may be another limitation.

Unexpected seizures and fear of being damaged, feeling anxiety from being ashamed as a result of losing control, conditioning as a result of traumatic seizures developed previously, and fear of stigmatization may cause both patients and their cohabiting relatives to feel fear and avoid the community. Thus, these patients and their cohabiting relatives could be reintegrated into society if these problems could be recognized and treated. Our study showed that both patients with epilepsy and their relatives have higher levels of anxiety compared with healthy control subjects. We emphasize the importance and necessity of recognizing and treating both groups to prevent them from being excluded from society. Apart from our study, the studies in the literature have been applied only in the mothers of patients with epilepsy; therefore, further studies in different groups of relatives and in more subjects would provide more decisive information on anxiety in patients with epilepsy and their relatives.

TABLE 5. Comparison of Scale Scores Among First-Degree Relatives[a]

Cohabiting Relative	LSAS		BAI	BDI	STAI-I	STAI-II
	Anxiety	Avoidance				
Mother	51.7±12.1	50.7±11.98	20.8±11.9	18.3±11.9	47±13.8	51.2±10.2
Father	35±16.5	35±16.5	13.3±10.6	13.3±8.15	38.7±18.5	45.3±17.6
Partner	46.3±12	47.9±12.4	12.6±6.7	10.7±6.4	37.8±12.5	42.6±7.3
Brother/sister	55.7±17	57±17.7	7.5±9.2	9±8.49	33±3.46	41.3±10.4
Total	48.4±13	48.8±13	15.9±10.3	14±9.79	41.5±13.7	46.2±10

[a] Data are presented as the mean ± standard deviation. BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; LSAS, Liebowitz Social Anxiety Scale; STAI, State-Trait Anxiety Inventory.

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