

ANXIETY IN EPILEPTIC PATIENTS

Milutin Nenadović¹, Miroslava Jašović-Gašić^{2,3}, Sreten Vičentić⁴,
Nenad Nenadović⁵ & Periša Simonović⁶

¹Special Psychiatric Hospital Laza Lazarevic, Belgrade, Serbia

²Faculty of Medicine, University of Belgrade, Clinic for Psychiatry, Clinical Center of Serbia, Belgrade, Serbia

³School of Medicine, University of Belgrade, Belgrade, Serbia

⁴Department of Psychiatry, General Hospital, Sabac, Serbia

⁵Military Medical Academy, Belgrade, Serbia

⁶Institute of Mental Health, Belgrade, Serbia

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SUMMARY

Background: Anxiety may occur as ictal, postictal or interictal symptom in patients with epilepsy. The main aim of this research was to explore the intensity and frequency of anxiety in patients with generalized, temporal and extratemporal epilepsy.

Subjects and methods: This is a cross-sectional study of three groups of patients with epilepsy (30 patients per group) - recently diagnosed with generalized epilepsy, temporal epilepsy and extratemporal epilepsy, and a healthy control group (N=30). The Beck Anxiety Inventory (BAI) was used for quantitative assessment of anxiety.

Results: Patients with temporal and extratemporal epilepsies had a significantly higher mean total scores on the BAI than the patients with generalized forms of epilepsies (ANOVA: $F=6.323$, $p<0.01$). There were no statistically significant differences between the temporal and extratemporal epilepsy groups according to the levels of anxiety on BAI (t -test: $t=1.68$, $p>0.05$). For the first three symptoms - numbness, wobbling in the legs and the fear of the worst happening - the group of patients with extratemporal epilepsies had significantly higher average levels of intensity and frequency of symptoms (ANOVA: $F_1=5.591$, $F_2=6.555$, $F_3=5.906$; $p<0.01$)

Conclusions: Patients with partial epilepsy have more frequent and prominent anxiety symptoms than patients with generalized epilepsy, and also more than the control group. All these findings clearly indicate the necessity to modify treatment strategies accordingly in order to include both the antiepileptic therapy and treatment for anxiety disorders.

Key words: anxiety - temporal epilepsies - extratemporal epilepsies - generalized epilepsies

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INTRODUCTION

The complex relationship between anxiety and epilepsy may be discussed individually for the same patient, through the following relations - anxiety as a reaction to a diagnosis of epilepsy, anxiety as a response to social and family stigma due to epilepsy, anxiety as an epileptic aura, ictal anxiety, anxiety (agitation) which occurs during epileptic psychosis, "organic" anxiety (in the case of psychoorganic syndromes), real phobic anxiety related to the attack and anxiety that precipitates an attack (Feddersen et al. 2005, Herman et al. 2000, Martinovic 1997). It's known that anxiety as an aura, can be the beginning of ictal experience in complex partial seizures. The theory of common pathophysiologic mechanism of anxiety attacks and seizures and epilepsy is based on observations that the epileptic activity in certain brain regions directly causes paroxysmal anxiety (Benbadis et al. 2001, Blumer 2000, Paesschen et al. 2001). The ictal fear is perhaps one of the clinically most important phenomenon when it comes to the relationship between anxiety and epilepsy. As an addition to this theory, there is a research that showed that even more than 50% of patients with an MRI confirmed atrophy of the amygdalae, had some forms of ictal fear (Paesschen et al. 2001). When one

talks about anxiety in epilepsies it is useful to make a distinction between ictal, postictal, interictal anxiety symptoms and comorbid anxiety disorders (Moore 1997, Mungas 1982). Contingency of anxiety symptoms with ictal epileptic discharges is the clearest if anxiety occurs in a repetitive manner, and immediately (a few seconds or minutes) before manifestation of a complex partial attack (Vazquez & Devinsky 2003). Postictal anxiety occurs in the period shortly after the epileptic seizure and is associated with confusion after recovering from the attack. Ictal anxiety is not common (Gaitatzis et al. 2004) and is usually combined with postictal dysphoria or depression (Kiely et al. 2010, Strine et al. 2005). It is possible that pure anxiety appears without other symptoms, but generally it is a combination of depression and anxiety disorders (Kanner et al. 2004, Lambert & Robertson 1999). In about 20% of patients with resistant forms of epilepsy the occurrence of phobias is registered (Gaitatzis et al. 2004). Most frequently it is agoraphobia or specific phobia of epileptic seizures. The fact is that diagnostic distinction of interictal anxiety and independent comorbid anxiety disorder is often difficult, especially if anxiety symptoms are not closely related in time with an epileptic occurrence (Vazquez & Devinsky 2003). Therefore, although the topic of the relationship

between anxiety and epilepsy is represented in literature worldwide, comparative data for different forms of epilepsies are scarce. Also, not enough consideration was given to frequency of individual anxiety symptoms, which could be indicators with certain diagnostic and prognostic value. Clarification of the abovementioned problems, in addition to existing know-how, would help formulate better both preventive and therapeutic strategies. The primary aim of our research is quantitative analysis of anxiety in patients with generalized epilepsies, focal temporal epilepsy and focal extratemporal epilepsy, and subsequently qualitative analysis of anxiety in the same groups of patients, according to the type of anxiety symptoms present. The main hypotheses are that all groups of patients with epilepsy will have a higher level of anxiety and more anxiety symptoms than subjects in the control group. Secondly, the group of patients with partial epilepsy of temporal lobe and the group with partial extratemporal epilepsy will have higher level of anxiety and more anxiety symptoms than the patients with generalized epilepsies.

SUBJECTS AND METHODS

This is a cross-sectional study of three groups of patients with epilepsy - patients recently diagnosed with generalized epilepsy (N=30), epilepsy of temporal lobe (N=30), and epilepsy of extratemporal localization (N=30). The control group consisted of 30 healthy subjects. The study was performed at the Institute of Mental Health in Belgrade, Department of Epilepsy and Clinical Neurophysiology, outpatient unit, during 2009. Study subjects in the four abovementioned groups were matched according to age and gender.

Criteria for inclusion were: 1) age 18 - 65 years, 2) diagnosis with one of the following: generalized, focused, symptomatic, probable symptomatic or idiopathic epilepsy.

Exclusion criteria included comorbidity of: 1) major depression, schizophrenia or bipolar disorder, 2) Addison's disease, active thyroid disease or instable diabetes, 3) intensive renal, cardiological, hepatic or gastrointestinal disease, 4) intensive neurological disorder, including parkinsonism and dementia, 5) pheochromocytoma, 6) urinary retention or closed angle glaucoma, 7) alcohol or drug abuse, 8) isolated seizures of any genesis, 9) epilepsy in mental insufficiency.

The Beck Anxiety Inventory -BAI (Beck et al. 1988) was used for quantitative assessment of anxiety. The BAI was primarily designed to measure generalized anxiety and to distinguish between anxiety and depressive symptoms. It consists of 21 items, and questions are ranked on a scale from 0 - 3 (0 = no, 1 = mild, 2 = moderate, 3 = severe). Maximum score is 63. Scores of 0-7 correspond to minimal anxiety, 8-15 to mild, 16-25 to moderate and 26-63 to severe anxiety.

Qualitative analysis of anxiety referred to discovery of presence / absence of some anxiety symptoms, based on a comprehensive list of anxiety symptoms (numbness or tingling, feeling hot, wobbling in the legs, unable to relax, fear of the worst happening, vertigo or dizziness, tachycardia, unsteady, fright, nervous, feeling of choking, hands trembling, shaky / unsteady, fear of losing control, difficulty in breathing, fear of dying, scared, indigestion, faint / lightheaded, face flushed, hot/cold sweats).

Data analysis

Data analysis started with descriptive statistics which included the arithmetic mean and median of the mean values, and a measure of variability of standard deviation, coefficient of variation and standard error, as well as the minimum and maximum value. We used the Fisher's analysis of variance (ANOVA) to assess the significance of between-group differences in BAI scores and single-item values. Pairwise comparisons of the groups of patients with epilepsy were performed by using the post-hoc Student's t-test for two independent samples with Bonferroni correction. The threshold of statistical significance was set at 0.05.

RESULTS

The anxiety level in all three groups of patients with epilepsy was compared with the level of anxiety in the control group of healthy subjects.

Looking at the BAI total scores in all the four groups, we found a statistically significant difference (ANOVA: $F=6.323$, $p<0.01$) - the temporal lobe epilepsy and extratemporal epilepsy groups have nearly equal values of mean scores (mean±SD: 15.90 ± 14.66 vs. 15.86 ± 11.95), while the generalized epilepsy group has significantly lower levels of anxiety (6.70 ± 5.06), which are even lower than the values in the control group (7.96 ± 9.15). The results are shown in Figure 1.

Student's t-test for two independent samples with Bonferroni correction showed that the patients from the group with extratemporal epilepsies have statistically significantly higher levels of anxiety than the patients with generalized epilepsies (t-test: $t=2.516$, $p<0.05$). Secondly, the group of patients with temporal epilepsy score was significantly higher on the BAI than the group of patients with generalized forms of epilepsies (t-test: $t=3.063$, $p<0.01$). There was no difference between the temporal and the extratemporal epilepsy groups (t-test: $t=1.68$, $p=1.00$) (Table 1).

The next level of testing was related to the analysis of individual symptoms of anxiety from the Beck Anxiety Inventory among the four study groups. Results are shown in the following Table 2.

The only items from the BAI that are showed here are those for which there is a statistically significant difference.

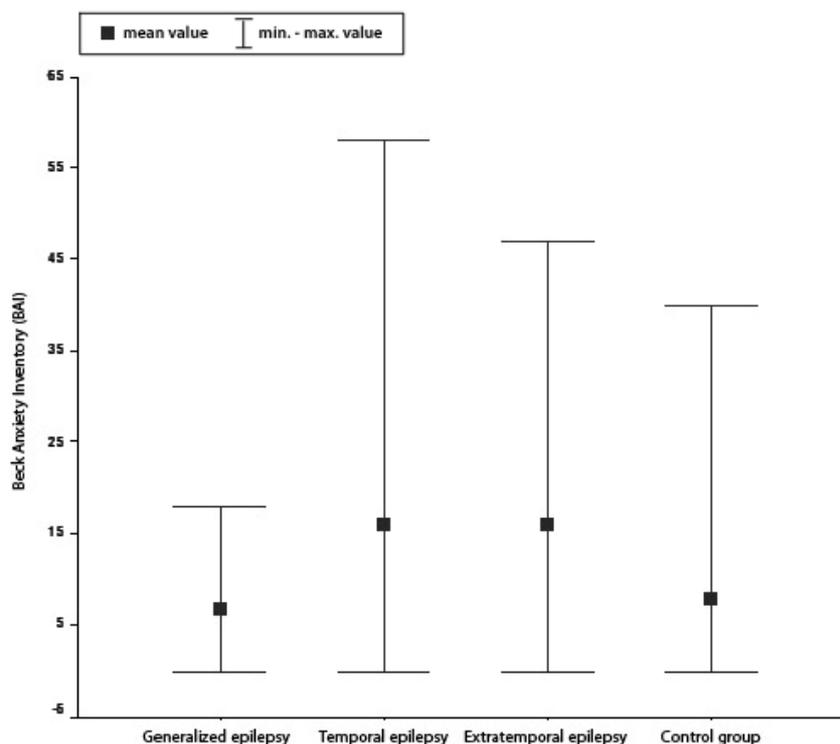


Figure 1. Average values of Beck Anxiety Inventory in all the observed groups

Table 1. Intergroup comparisons of mean values on BAI by using the post-hoc Student's *t*-test for two independent samples with Bonferroni correction

Epilepsy group	Difference of Means	SE	t	p
Extratemporal/Generalized	8.58	3.41	2.516	0.041
Temporal/Generalized	10.26	3.35	3.063	0.009
Extratemporal/Temporal	1.68	3.40	0.494	1.000

Table 2. Comparison of anxiety symptoms between the observed groups

Beck Anxiety Inventory	G 1	G 2	G 3	G 4	F	p
Numbness or tingling	0.13	0.56	0.73	0.16	5.591	0.001
Wobbling in the legs	0.23	0.70	0.96	0.23	6.555	0.0001
The fear of the worst happening	0.36	0.93	1.13	0.30	5.906	0.001
Vertigo or dizziness	0.26	0.60	0.80	0.40	3.004	0.033
Tachycardia	0.30	0.90	0.63	0.46	3.281	0.023
Unsteady	0.26	0.90	0.76	0.23	6.841	0.000
Terrified or afraid	0.20	0.63	0.70	0.30	2.981	0.034
Nervous	1.20	1.63	1.63	1.10	3.399	0.020
Shaky/unsteady	0.20	0.43	0.70	0.23	3.075	0.030
Fear of losing control	0.16	0.70	0.93	0.40	4.295	0.007
Scared	0.16	0.70	0.83	0.23	5.352	0.002
Faint/lightheaded	0.06	0.73	0.46	0.16	6.191	0.001

G 1 - mean value in generalized epilepsies group; G 2 - mean value in temporal epilepsies group; G 3 - mean value in extratemporal epilepsies group; G 4 - mean value in the control group

Table 2 shows that the group of patients with extratemporal partial epilepsies have significantly higher average levels of intensity and frequency of the first three symptoms - numbness, wobbling in the legs and the fear of the worst.

Patients with temporal lobe epilepsy also have high average values of these three symptoms, while patients with generalized epilepsy have much lower average scores (mean±SD: 0.56±0.85 vs. 0.13±0.34, ANOVA: F=5.59, p<0.01). The symptom of vertigo is also

common in patients with extratemporal partial epilepsies, somewhat rarer / less expressed in patients with temporal lobe epilepsy and the least expressed in the generalized epilepsies. The differences are statistically significant (0.80 ± 0.88 vs. 0.60 ± 0.89 vs. 0.26 ± 0.44 , ANOVA: $F=3.004$, $p<0.05$). The last two physical symptoms of anxiety - tachycardia and unsteadiness are more frequent / intense in patients with temporal lobe epilepsy compared to extratemporal epilepsies which differs from the previous general trend. The difference is statistically significant for the symptom of tachycardia (0.90 ± 0.92 vs. 0.63 ± 0.88 , ANOVA: $F=3.281$, $p<0.05$) and highly statistically significant for the symptom of unsteadiness (0.90 ± 0.92 vs. 0.76 ± 0.85 , ANOVA: $F=6.841$, $p<0.01$).

Table 2 also shows that the statistically significant differences (at the level of $p=0.01$) between the observed groups are present for the symptoms of faintness, fear of losing control and fright. Faintness is the most common / most noticeable in patients with temporal lobe epilepsy, somewhat less in extratemporal epilepsies, and the least in generalized epilepsies. The difference is statistically highly significant (ANOVA: $F=6.191$, $p<0.01$). The fear of losing control and fright are the greatest in patients with extratemporal epilepsies. These two symptoms are less noticeable in patients with generalized epilepsies than in the control group. The feeling of being terrified and shivers are most pronounced in patients with extratemporal partial epilepsies which follows the overall trend of those being the other most common symptoms of anxiety. However, anxiety as a general and nonspecific symptom is marked and equally present in all the three groups of patients with epilepsies, and slightly less in the control group (although even there it is more pronounced than it would be expected).

DISCUSSION

The basic hypothesis of this study - that the groups of patients with epilepsy have a higher level of anxiety and more anxiety symptoms than the subjects in the control group is only partially confirmed. The hypothesis is confirmed only when patients with partial extratemporal epilepsies and with temporal lobe epilepsy were compared to the healthy control group. This finding is in agreement with data showing that prevalence of anxiety disorders in patients with temporal lobe epilepsy is significantly higher than in the general population and is estimated at 19% (Beyenburg et al. 2005). However, when it comes to patients with generalized epilepsy, frequency and intensity of the most of anxiety symptoms is equal to or even lower than in the control group subjects. In this study we have used the Beck Anxiety Inventory to explore the phenomenon of anxiety, and its validity and reliability has been well documented (Fydrich et al. 1992). A special advantage of this questionnaire is the possibility to differentiate

anxiety symptoms from depression, which was very important for our research. It is true that anxiety and depression are often present together, but when one talks about this comorbidity it should be known that anxiety can often be found without the presence of depression, but the opposite is not the case (Murphy et al. 2004). In our study, the unexpectedly similar finding of anxiety levels in the group with generalized epilepsies and the control group, was probably caused by the relatively small sample size.

One of our hypotheses is that the group of patients with partial temporal lobe epilepsy and with partial extratemporal epilepsies will have higher levels of anxiety and more anxiety symptoms than patients with generalized epilepsies. This hypothesis has been proved correct. Specifically, patients with temporal epilepsy as well as partial extratemporal epilepsies had a significantly higher overall scores on the BAI compared to the group of patients with generalized epilepsies (Table 1 and 2). The difference between the temporal / generalized epilepsy groups was statistically highly significant ($p<0.01$), and the difference between the extratemporal / generalized epilepsy groups was also statistically significant, but to a ($p<0.05$). This finding is in accordance with the reports from the literature that the risk of anxiety disorders is higher in focal epilepsies (especially the temporal lobe epilepsy) than in generalized epilepsies (Marsh & Rao 2002, Goldstein & Harden 2000). Furthermore, Vasquez and Devinsky found that anxiety and depression are more common in epilepsy of the temporal and frontal lobes than in idiopathic generalized epilepsies (Vasquez & Devinsky 2003).

Our results are in agreement with the work of Brandt and associates, who found that patients with refractory partial epilepsies more often have comorbid anxiety disorders. The authors relate this, among other things, to the level of seizure control, i.e. patients with focal epilepsies generally have poorer seizure control than patients with generalized epilepsies (Brandt et al. 2010). Our qualitative analysis of individual anxiety symptoms of the Beck's questionnaire show that the frequency and intensity of certain anxiety symptoms are higher in patients with partial extratemporal epilepsies and temporal lobe epilepsies than in the generalized epilepsy. Moreover, frequency and intensity of anxiety symptoms in patients with generalized epilepsy is equal to or even lower than that in the control group. If we single out particular anxiety symptoms that prevail in patients with partial epilepsy, we can see that what is left are most frequently somatic symptoms such as vertigo, faintness, numbness / tingling, unsteadiness, tachycardia, shivers as well as the fear of losing control and anticipation of the worst happening. Therefore we can indirectly conclude that the described phenomenology can represent or be a part of a panic disorder or symptoms of generalized anxiety. This finding correlates with the data from the literature about particularly high incidence of panic attacks in patients with epilepsy. Some studies have shown that patients

with epilepsy are six times more likely to have panic attacks than those from the general population (Vazquez & Devinsky 2003, Marsh & Rao 2002).

It is interesting to notice that when it comes to individual symptoms - numbness, uncertainty in the legs, fear of the worst happening and faintness - the group of patients with partial extratemporal epilepsies showed significantly higher average intensity levels and frequency of symptoms than the group with temporal lobe epilepsies, which is different from the BAI total scores in these groups. This finding may indicate the future need for designing more extensive comparative studies, which would examine the relationship between anxiety in these two groups in more details. Treatment of anxiety in patients with epilepsy involves identification and quantitative and qualitative analysis of the presence of anxiety symptoms, their correlation with epileptic seizures (ictal, ante-periictal, interictal symptoms) and/or antiepileptic therapy, according to one of the two dominant systems of classification of anxiety disorders, ICD 10 (World Health Organization 1992) or DSM-IV (American Psychiatric Association 1994). When the anxiety disorder is diagnosed in people with epilepsy, then the anxiety disorder should be noted as well. Integrative approach to diagnosing the condition in patients obliges one to an integrated treatment of patients with epilepsy. Such a holistic approach (pharmacological, psychological and socio-therapeutic measures) in treatment and prevention of symptoms in patients with epilepsy increases the performance of the final results of therapy.

CONCLUSION

The patients with temporal lobe epilepsy have a higher overall scores on the Beck Anxiety Inventory than the patients with generalized epilepsy, the difference being highly significant. Furthermore, the patients with extratemporal epilepsies have higher scores, and the difference is statistically significant. Among the patients with temporal lobe epilepsy and extratemporal epilepsies there is no statistically significant difference in total scores on the BAI. Comparison of anxiety symptoms between the groups of patients with epilepsy has shown that patients with partial epilepsy have more frequent and pronounced anxiety symptoms than the patients with generalized epilepsy. Research indicates therapeutic guidelines for anxiety in patients with epilepsy.

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Correspondence:

Miroslava Jašović-Gašić, MD, PhD, Professor of Psychiatry
Faculty of Medicine, University of Belgrade, Clinic for Psychiatry, Clinical Center of Serbia
Pasterova 2, 11000 Belgrade, Serbia
E-mail: mjasovicgasic0@gmail.com