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Focus Laterality and Interface Between Depression and Anxiety in Patients with Temporal Lobe Epilepsy

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Additional information is available at the end of the chapter

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Abstract

The aim of the current study was to evaluate an interaction between anxiety and depression in persons with temporal lobe epilepsy (TLE) in relation to foci lateralization. Ninety-four patients with temporal lobe epilepsy were included in the study (25 cases with left-sided focus activity, 25 cases with right-sided focus activity, and 44 patients with bilateral foci activity). The Hopkins Symptoms Check List (SCL-90) scale was used for psychopathological assessment. Pearson product moment correlations between nine constructs of SCL-90 were calculated separately for left-sided, right-sided, and bilateral foci groups. On the final stage, forward stepwise regression analysis was used for left-sided, right-sided, and bilateral foci groups separately. As dependent variables, the SCL-90 constructs of depression and anxiety were used. The obtained findings have shown the existence of close correlation between constructs of depression and anxiety in the right-sided focus and bilateral foci TLE patients, whereas the correlation was less expressed in the left-sided focus group. Regression analysis revealed the dependence of depression on anxiety and vice versa dependence of anxiety on depression in the right-sided focus group, but not the left-sided focus group. Depression and anxiety seem to represent one more solid syndrome in TLE patients with right-sided focus activity and rather two independent syndromes in TLE patients with the left-sided focus activity.

Keywords: temporal lobe epilepsy, focus laterality, affective disorder, anxiety disorder, SCL-90 constructs

1. Introduction

The concomitant psychopathological disorders, i.e., organic affective disorder and organic anxiety disorder are thought to be the most frequent co-morbid pathology in patients with temporal lobe epilepsy (TLE). Their frequency seems to achieve about 10–50% in TLE [1–6]. Nonetheless, the data on psychopathology of these states are scarce and rather controversial. It concerns the issue of possible relation between focus laterality and kind of prevailed affective symptoms in TLE. Thus, if some authors draw attention to the principal role of left temporal foci coupled with decreased functional state of frontal lobes in the genesis of depression, other researchers stress that the focus lateralization has no relation to the consequent affective disorder development [1–5].

Data on verified association between depression, anxiety and other concomitant symptoms and their interaction in TLE patients in relation with focus laterality are rather absent, although they could shed light on pathogenesis of affective and anxiety syndromes in terms of neuropsychiatry and evolution.

Here should be stressed that variables connected with right hemisphere are believed to be older and appear on earlier stage of phylogeny and ontogenesis, whereas the left hemisphere variables are much younger and appear on later stage of evolution [7]. If any discrepancies in certain signs and symptoms between both hemispheres existed, then probable evolutionary sequence of these variables could be suggested and their different role in mental disorders in terms of course and prognosis might be predicted.

In our previous study [8], we have shown that the diagnosis of organic affective disorder was observed more frequently in patients with right-sided foci, whereas the diagnosis of organic anxiety disorder in patients with left-sided foci ($\chi^2 = 7.0$ $p = 0.0081$; Fisher's exact test $p = 0.018$). In other words, the right-sided focus determines the symptoms of depression, whereas the left-sided focus causes the symptoms of anxiety in interictal period in TLE. In evolutionary terms, it implies that depression is older disorder than anxiety. Nevertheless, the certain co-morbidity between anxiety and depression exists in TLE patients with left-sided focus, and in lesser degree in patients with right-sided focus, and co-morbid anxiety and depression states usually appear more frequently in patients with left-sided focus activity [9, 10].

Principally, the similar association is true for patients with stroke, and persons with left hemisphere stroke are characterized by mixed anxiety and depressive symptoms in the form of the so-called catastrophic reaction (term proposed by Kurt Goldstein) compared with patients with right hemisphere stroke in whom the depression with prominent indifference usually appears [11–13].

2. Objective

The main aim of the current study was to evaluate an interaction between different psychopathological constructs (with principal emphasis on anxiety and depression) in persons with TLE in relation to focus lateralization.

3. Material and methods

The study has been carried out on 94 patients with TLE. Among all, studied patients were 38 men and 56 women. The focus laterality was detected strictly by visual EEG method, and data on ictal semiotics have not been used for this purpose. The left-sided foci were detected in 25 (11 men, 14 women) patients, the right-sided foci in 25 (11 men, 14 women) patients, and the bilateral foci in 44 (16 men and 28 women). The symptomatic form of TLE was diagnosed in 40 patients, and cryptogenic form in 54 patients.

All patients were evaluated by psychiatrists in order to set a psychiatric diagnosis. ICD-10 criteria were used for these purposes. In line with these criteria, the next disorders were diagnosed: (1) organic affective disorder (F06.3) (24 patients) and (2) organic anxiety disorder (F06.4) (48 patients).

Along with above-mentioned ICD-10 criteria, the diagnosis of “Interictal dysphoric disorder” also was used (22 patients), although it was not represented in ICD-10.

The rating of psychopathological symptoms of Hopkins Symptoms Check List (SCL-90) scale has been performed by patients themselves [14, 15]. Raw data of SCL-90 were then transformed into nine constructs that have been included in the final analysis of interaction between affective and anxiety syndromes. In accordance with SCL-90 design, the next nine constructs have been created: “somatization”, “obsessive-compulsive”, “interpersonal sensitivity” “depression”, “anxiety”, “hostility”, “phobic anxiety”, “paranoid ideation”, and “psychoticism” [14, 15].

AED	Left-sided focus Mean daily dose and number of patients	Right-sided focus Mean daily dose and number of patients	Bilateral Foci Mean daily dose and number of patients
Topiramate	115.63±39.93 (n=8)	116.67±35.36 (n=8)	133.93±33.41 (n=14)
Valproates	1133.33±321.45 (n=5)	1105±520.42 (n=4)	1051.25±329.92 (n=13)
Carbamazepine	962.50±320.43 (n=8)	800.0±244.95 (n=8)	700.0±229.98 (n=10)
Phenobarbital	100.0±70.71 (n=4)	150.0±70.71 (n=5)	115.71±77.05 (n=7)

Table 1. Used antiepileptic drugs and their daily doses in studied patients.

All patients continued to intake antiepileptic drugs (AEDs) as monotherapy. The principal data on AEDs are listed in **Table 1**.

4. Statistics

All data were statistically processed by Statistica program (6th version) on personal computer. Student's *t*-test was performed on the first step for comparison of means of SCL-90 constructs in left-, right-sided foci, and bilateral foci groups.

The correlation analysis was chosen for purpose of evaluation of associations between the different psychopathological syndromes, and the product moment correlation (Pearson correlations) between all SCL-90 constructs was obtained separately within group with left-sided and right-sided foci activity for this purpose. The ratings of correlation between SCL-90 constructs have been compared between studied groups for purpose to find any possible discrepancies between them. A suggestion has been made that the closer correlation between two variables, the more common mechanism in their origin they have.

On the final stage, the multiple regression analysis (forward stepwise regression) was used for left-sided, right-sided, and bilateral foci groups separately. Multiple regression analysis has been selected as optimal for study of joint effect of a number of different factors on outcome variable [16, 17]. As dependent variables, the SCL-90 constructs of depression and anxiety subsequently were used.

5. Results

The principal results are depicted in **Tables 1–7**. In **Table 1**, the mean daily doses of AEDs are shown, and no statistically significant differences between compared groups are observed. In **Table 2**, the mean values of SCL-90 constructs are listed. No significant discrepancies between left-sided-, right-sided-, and bilateral foci groups on SCL-90 constructs have been obtained. It implies that focus lateralization has no influence on the expression of each SCL-90 construct, and their rates in both groups were practically equal.

SCL-90 construct	Left-sided focus	Right-sided focus	Bilateral foci
Somatization	8.78±5.64	6.43±5.24	7.07±6.38
Obsessive-compulsive	8.82±5.56	9.17±9.9	7.63±6.57
Interpersonal sensitivity	7.26±6.21	6.65±4.94	7.68±6.17
Depression	8.43±7.11	7.78±6.87	7.39±6.52
Anxiety	6.26±4.27	6.73±6.98	5.66±5.49
Aggressiveness & Hostility	3.65±2.87	4.52±4.25	4.20±3.52
Phobia	3.35±3.78	2.78±2.58	3.07±3.25
Paranoid ideations	3.48±3.88	4.00±4.34	3.70±3.34
Psychoticism	3.22±3.84	3.65±4.87	3.36±4.23

No statistically significant discrepancies were obtained.

Table 2. Values of SCL-90 constructs (Mean± Std.Dev.) in TLE patients with left-right-sided and bilateral activity.

	Somatization	Obsessions	Sensitivity	Depression	Anxiety	Hostility	Phobia	Paranoid ideations	Psychoticism
Somatization	-	0.68	0.40	0.39	0.78	0.51	0.44	0.49	0.62
Obsessions		-	0.81	0.84	0.78	0.74	0.71	0.68	0.65
Sensitivity			-	0.80	0.67	0.62	0.72	0.77	0.43
Depression				-	0.60*	0.79	0.53*	0.52	0.65
Anxiety					-	0.74	0.62	0.77	0.68
Hostility						-	0.34	0.64	0.78
Phobia							-	0.55	0.34
Paranoid ideations								-	0.51*
Psychoticism									-

Note: significant Pearson product moment correlation ($p < 0.05$) are marked by bold.

Table 3. Correlation matrix of SCL-90 constructs in TLE patients with left-sided focus.

	Somat	Obses	Sensit	Depres	Anxiety	Hostility	Phobia	Paranoid	Psychot
Somat	-	0.80	0.73	0.77*	0.85	0.62	0.58	0.73	0.86*
Obses		-	0.69	0.69	0.77	0.59	0.65	0.83	0.93*
Sensit			-	0.75	0.58	0.55	0.49	0.68	0.75*
Depres				-	0.85	0.80	0.28	0.80	0.66
Anxiety					-	0.78	0.51	0.87	0.80
Hostility						-	0.22	0.71	0.60
Phobia							-	0.59	0.73*
Paranoid								-	0.79*
Psychot									-

Note: significant Pearson product moment correlation ($p < 0.05$) are marked by bold.

* - statistically significant differences in Pearson correlation between patients with left-sided focus and right-sided focus activity.

Table 4. Correlation matrix of SCL-90 constructs in TLE patients with right-sided focus.

	Somat	Obses	Sensit	Depres	Anxiety	Hostility	Phobia	Paranoid	Psychot
Somat	-	0.46*	0.58	0.72[§]	0.78	0.52	0.61	0.30*	0.53*
Obses		-	0.58[§]	0.54[§]	0.47^{§*}	0.41[§]	0.47	0.41*	0.50*
Sensit			-	0.77	0.73	0.79	0.77	0.66	0.75
Depres				-	0.82	0.71	0.75	0.59	0.83

	Somat	Obses	Sensit	Depres	Anxiety	Hostility	Phobia	Paranoid	Psychot
Anxiety					-	0.64	0.74	0.46*	0.64
Hostility						-	0.85	0.71	0.83
Phobia							-	0.74	0.77
Paranoid								-	0.76
Psychot									-

Note: significant Pearson product moment correlation ($p < 0.05$) are marked by bold.
*- statistically significant differences in correlations between bilateral foci group and right-sided focus group.
§- statistically significant differences in correlations between bilateral foci group and left-sided focus group.

Table 5. Correlation matrix of SCL-90 constructs in TLE patients with bilateral foci.

In **Tables 3–5**, the correlation matrixes are shown for all SCL-90 constructs separately for groups with left-sided (**Table 3**), right-sided (**Table 4**), and bilateral focus activity (**Table 5**).

As can be seen in patients with right-sided focus, as a whole, the values of Pearson product moment correlation were higher than in the left-sided and bilateral group. Comparison between right-sided and left-sided groups revealed that the correlations between depression and other constructs, such as somatization ($r = 0.77$ versus $r = 0.39$), anxiety ($r = 0.84$ versus $r = 0.61$), and paranoid ideations ($r = 0.78$ versus $r = 0.54$) were higher in patients with the right-sided focus. Comparison of the right-sided focus patients with patients with bilateral foci also revealed higher correlations between somatization on the one hand, and obsessions ($r = 0.80$; $p < 0.01$), paranoid ideations ($r = 0.73$; $p < 0.01$), and psychoticism ($r = 0.86$; $p < 0.01$), on the other hand, in the right-sided focus group. Similarly, the correlation between anxiety and paranoid ideations was higher in the right-sided focus group ($r = 0.87$; $p < 0.001$) than in the bilateral foci group ($r = 0.46$; $p < 0.01$).

On the contrary, the correlation between depression and phobia was higher in the bilateral foci patients ($r = 0.75$; $p < 0.01$), than in the right-sided focus group ($r = 0.28$; n.s.) and left-sided focus group ($r = 0.53$; $p < 0.01$). In the right-sided focus patients, the associations of depression seem to be higher with somatization, anxiety, and paranoid ideations and less with phobia in comparison with the left-sided focus patients.

Data on the multiple regression analysis are listed in **Tables 6** and **7**. In **Table 6**, the results of multiple regression analysis for depression as dependent variable for three compared groups are presented. As can be seen, certain discrepancies between groups exist. In TLE patients with right-sided foci, the depression score was determined by rate of anxiety, obsessions, and interpersonal sensitivity, whereas the psychoticism reduced the final score of depression.

Similarly in the group with left-sided focus, the level of depression was determined by rate of obsessions and interpersonal sensitivity. Nonetheless, unlike the persons with right-sided focus, in patients with left-sided focus anxiety has not been interrelated with depression. In addition, a high level of paranoid ideations finally reduced score of depression. In other words, in patients with the left-sided foci depression and anxiety seem to be independent variables, whereas in the right-sided foci patients these constructs are interconnected.

Item	TLE patients with left-sided focus	TLE patients with right-sided focus	TLE patients with bilateral foci
Intercept	-0.324	-0.808	1.123
Somatization SCL-90	-0.240	-	0.158
Obsessions SCL-90	+0.476	+0.438	-
Interpersonal Sensitivity SCL-90	+0.520	+0.592	-
Anxiety SCL-90	-	+0.839	+0.366
Hostility and Aggression SCL-90	+0.320	-	-
Phobic anxiety SCL-90	-	-0.210	-
Paranoid Ideations SCL-90	-0.370	-	-
Psychoticism SCL-90	+0.216	-0.710	+0.513

Table 6. Forward stepwise regression analysis (values of beta coefficients) for the depression (SCL-90), as dependent variable in group with left-, right-sided and bilateral foci.

Item	TLE patients with left-sided focus	TLE patients with right-sided focus	TLE patients with bilateral foci
Intercept	+0.345	+1.268	-0.610
Somatization SCL-90	+0.466	+0.246	+0.314
Obsessions SCL-90	-0.220	-0.460	-
Interpersonal Sensitivity SCL-90	-	-0.500	+0.174
Depression SCL-90	-	+0.545	+0.478
Hostility and Aggression SCL-90	+0.400	-	-
Phobic anxiety SCL-90	+0.292	-	+0.243
Paranoid Ideations SCL-90	+0.271	+0.448	-
Psychoticism SCL-90	-	+0.701	-0.240

Note: Statistically significant values of beta coefficients are marked by bold.

Table 7. Forward stepwise regression analysis (values of beta coefficients) for the anxiety (SCL-90), as dependent variable in group with left-, right-sided and bilateral foci.

In the bilateral foci group, the rate of depression was determined by level of anxiety and psychoticism, and this implies that all these constructs are interconnected.

Similar findings on interaction between depression and anxiety were obtained based on regression analysis data when the anxiety was selected as dependent variable (**Table 7**). In the right-sided foci TLE patients, the final rate of anxiety was determined by the level of depression, and in addition by paranoid ideations and psychoticism, whereas the interpersonal sensitivity and obsessions reduced the final score of anxiety.

In the bilateral foci group, the rate of anxiety depends on the level of depression and somatization, whereas in the group with the left-sided foci, the level of anxiety was independent on depression, but was determined by constructs of somatization, hostility, aggression, phobic anxiety, and paranoid ideations.

6. Discussion

The current study was designed in order to analyze the influence of foci laterality in patients with temporal lobe epilepsy on psychopathological variables of SCL-90 with special emphasis on interaction between depression and anxiety. The study has certain limitations, and may be criticized for the lack of special psychometric scales, i.e., Hamilton rating scales for depression and anxiety. The psychometric quantified scales and the psychometric data have not been taken into account in the present study, since the controversial rate for their use exists, and some authors argue against their expansive use in psychiatry [18–20].

To our knowledge, this is the first attempt to analyze the effect of foci laterality on interaction between anxiety and depression in patients with TLE.

The main findings have shown that the right and left foci have an unequal effect on linkage between depression and anxiety in patients with TLE, although there has not been observed any effect of foci on mean average of any SCL-90 constructs. Moreover, as has been observed, the mean daily doses of used antiepileptic drugs had no statistically significant influence on the left-sided, the right-sided, and bilateral foci patients. It implies that obtained findings could not been caused by AEDs effect itself.

The principal results have shown that in patients with TLE with the right-sided focus and bilateral foci the closer association between symptoms of anxiety and depression exist, whereas in patients with left-sided foci this correlation is much less expressed. Moreover, multiple regression analysis could not reveal any statistically significant influence of anxiety on depression and vice versa in patients with left-sided foci, although the stable constellation of constructs including depression, interpersonal sensitivity, and obsessions was revealed in each hemisphere irrespective of focus laterality. It concerns strictly patients with unilateral foci, but not with bilateral foci. It implies the stable cluster pattern of depression, obsessions, and interpersonal sensitivity both in the right-sided- and in the left-sided focus patients can exist. Taking these data together, suggestion can be made that in the right-sided foci patients the more solid syndrome of depression with anxiety develops, whereas in the left-sided focus cases the looser associations between both disorders exist. In other words, in the cases of right-sided foci we may suggest the development of single poor differentiated syndrome, consisting of both depression and anxiety. On the contrary, in the patients with left-sided foci rather two independent syndromes (depression and anxiety) usually originate, and the so-called comorbidity of depressive-anxiety disorders exists.

Despite the outer similarity in psychopathological symptoms in TLE patients with left-sided- and right-sided focus activity, the definite inner discrepancies in origin mechanisms of studied

psychiatric disorders exist in relation to focus laterality. Probably, these discrepancies could explain the variability of drug responses in cases with externally similar affective and anxiety disorders, since their hemispheric origin is not usually taken into account. Psychiatric disorders with right hemisphere origin (in TLE patients with right focus activity) hypothetically are thought to be more favorable for antidepressant treatment, than disorders with left hemisphere origin (TLE patients with left focus activity), since the existence of two or more independent syndromes with different pathogenesis in the left-sided focus patients could be suggested, although this should be proven in a special study.

Data on correlation analysis in TLE patients with bilateral foci activity seem to be similar to findings on TLE patients with right-sided focus, and practically similar correlations between constructs of depression and anxiety in these groups exist. Obviously, the right-sided focus in patients with bilateral foci continues to have impact on syndrome genesis in manner similar to patients with definite right-sided- but not left-sided foci, although it concerns strictly constructs of depression and anxiety.

In our previous study, the preponderance of depression in patients with right-sided foci was observed. On the other hand, the higher frequency of anxiety disorder in patients with left-sided foci was obtained [8]. At the first glance, the certain contradiction with the findings of the current study exists. This contradiction seems to be explained by different methods used in these studies. Thus, in previous work [8], the diagnosis was made exclusively based on psychiatrists observations and data by Hamilton's rating scales for depression and anxiety were also used supplementary to physician decisions. In the present study, the subjective data of patients on the SCL-90 questionnaire were the corner stone of trial design. The more solid right-sided syndrome in the present study could be regarded by physicians as depressive one, although it may have as depressive, as anxiety symptoms. On the other hand, the left-sided syndrome due its more definite anxiety symptoms, independent of depression could be considered by psychiatrists as anxiety disorder, although it remains as pure speculative suggestion.

The rule, proposed Geodakian asserts, that signs and symptoms, associated with right hemisphere are older, than signs linked with left hemisphere [7]. In accordance with this paradigm, we may suggest that more monolithic depressive-anxiety syndrome revealed in cases with right-sided foci in evolutionary terms is older, than independent depression and anxiety, attributed to left hemisphere. Taking all these data, conclusion can be made on evolutionary direction of some psychopathological syndromes. The evolution of psychopathological signs goes from right hemisphere with less differentiated syndromes through bilateral foci to the left hemisphere with more differentiated signs, although this suggestion is thought to remain purely speculative. The independent anxiety and depression syndromes seem to be a prerogative of the left hemisphere. The current study should be continued in order to shed light on evolution of other psychopathological syndromes. Obtained findings stress the role of foci laterality in interaction between of depressive and anxiety syndromes in TLE, and may be presumably extrapolated on brain mechanisms of affective and anxiety disorders irrespective of epilepsy. If the proposed hypothesis was true, the right hemisphere involvement in the mechanisms of less differentiated symptoms of depression and anxiety and

the left hemisphere involvement in the genesis of two separate syndromes of anxiety and depression should be suggested, although that speculative assumption should be proved in special studies.

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