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Neurobiological and Personality Risk Factors for Development of Obsessive-Compulsive Disorder in Patients with Epilepsy

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1. Introduction

Psychiatric co-morbidities in forms of affective and anxiety disorders are believed to be the most frequent complications of epilepsy. It concerns mostly the patients with localization related forms, and temporal lobe epilepsy [TLE], in particular. Perini et al. have shown that patients with TLE have higher rates of affective and personality disorders compared to persons with juvenile myoclonic epilepsy [1]. Despite their frequent prevalence that achieves about 8%-50% among patients with epilepsy [2-6] the data on the risk factors for the development of psychiatric co-morbidities in TLE remain obscure and rather controversial. That also concerns obsessive-compulsive disorder (OCD), which is regarded as one of co-morbid psychopathological complications in TLE [7].

According to Bear and Fedio data [8] focus laterality in TLE determines the kind of interictal psychopathology, and in patients with right-sided TLE such symptoms as sadness, elation and obsessional thinking can origin, while in the left-sided TLE paranoia, anger, dependence and negative self-image may appear.

Nevertheless, these results have been lately criticized since some subsequent studies couldn't replicate these data [9,10]. It implies that data on foci lateralization themselves couldn't explain the origin of some psychopathological signs and obsessional thinking in particular in all cases of TLE. Obviously some other neurobiological factors and personality traits should also be taken into account in order to predict the probable OCD development in TLE. Moreover, whether the seizure semiotics has influence upon its development or not remains unknown

although in 19-th century have been reported that obsessions were frequently accompanied by a family history of epilepsy [11, 12].

Among neurobiological factors the data on motor lateralization can be important for prediction of psychopathological comorbidity i.e. OCD. Along with neurobiological signs the personality structure variables also may be important for this reason.

Thus, focus lateralization in TLE is thought not to be enough to predict the probability of psychopathology development in patients with epilepsy, and other factors, such as motor lateralization and premorbid personality features also should be taken into account. In one of our previous study we have shown that Alexithymia exerts maximal effect on psychopathological variables, i.e. Depression in SCL-90, and maximal values of SCL-90 constructs were observed in cases with combination Alexithymia and left-handedness and Alexithymia and right-sided seizure focus [13]. Here should be stressed that Alexithymia itself represents only a part of complicated psychopathological structure of so-called premorbid personality, and other personality factors may be also important for the development of psychopathological disorders in patients with TLE. Any possible relationships between personality, neurobiological variables and OCD in epilepsy have not been properly studied.

Premorbid personality features to date have been fairly studied in terms of risk for psychiatric pathology in numerous studies. It concerned mainly the role of premorbid personality structure in affective disorders, schizophrenia, and organic disorders, although the strictly definite and universal findings have not been obtained yet. Thus, Tellenbach introduced concept of "Typus melancholicus" (TM) which is still regarded as premorbid personality features constellation for unipolar (recurrent) depression development [14-16]. Such approach has been mainly used in Germany and Japan and obtained in this context data are rather controversial, and complicated. Thus, if some authors agree in unison on the significant role of TM in depression development [14-17] other authors are careful and could find, that only between 30 and 70 % of depressed patients have a typical TM structure [18, 19].

Thus, Furukawa et al.[19] used a special scales for assessment of TM features in 140 psychiatric patients and couldn't find any statistically significant discrepancies with normal control subjects except that among the recurrent depression patients the TM score was lower than in control group. Unfortunately the similar study has not been performed in epilepsy patients yet, and whether the premorbid personality has influence on the development of psychopathology remains unknown.

To date the several personality traits are thought to be significant for the development of psychiatric disorders at all, and some tests have been elaborated in this context to detect such personality predisposition to depression in particular. One of such questionnaire widely known as Munich Personality Test (MPT) has been developed by von Zerssen et al using factor analysis in 1988 [20]. Detailed description of MPT is given in Materials and Methods section.

Although such multidimensional approach has been widely used in psychiatry, data on its use in patients with epilepsy are practically absent. Since such neuropsychological variables as focus laterality (FL) and motor lateralization (ML) are important for development of psychiatric disorders in patients with TLE [13], suggestion could be made that premorbid personality

features in patients with TLE might be significant for the development of comorbid psychopathology, and OCD in particular, if take into account their interaction between each other.

The principal aim of the current study was to find any possible relationships between personality features and OCD development in patients with different neurobiological patterns i.e. in persons with different combination of FL and ML. The corner stone of the current study was hypothesis, that the different combinations of FL and ML are thought to be a neurobiological basis for relationship between premorbid personality features, on the one hand, and obsessive-compulsive symptoms, on the other hand in patients with TLE.

2. Material and methods

The study has been carried out on 103 patients with epilepsy. Among all studied patients were 33 men and 70 women. The diagnosis of symptomatic epilepsy was set in 40 patients, the diagnosis of cryptogenic form –in 54 patients, and the diagnosis of idiopathic temporal lobe epilepsy-in 9 patients. The focus laterality was detected strictly by visual EEG-method, and data on ictal semiotics have not been taken into account. The left-sided foci were detected in 48 patients (12 men and 36 women), the right-sided foci – in 55 patients (22 men and 33 women).

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 diagnosis of OCD was set in 19 patients. For the assessment of severity of OCD symptoms the correspond construct of SCL-90 scale was used and filled in by physicians. The mean value of obsessive-compulsive construct in OCD patients reached 20,16+4,13, while in patients without OCD – only 6,31+3,72 points.

For assessment of the premorbid personality features the MPT has been used [20]. The MPT represents a self-rating questionnaire, and includes 51 questions depicting the different personality traits. The patients have filled in all rating scales themselves, and after that the obtained raw data have been transformed into six constructs in line with specific structure of scales. These constructs include Extraversion, Neuroticism, Rigidity, Frustration Tolerance, Tendencies to Isolation and Esoteric Tendency. The last two constructs form Schizoidia scale [20]. The other two control scales of MPT (Orientation towards Social Norms and Motivation) were not included in the final analysis.

Extraversion and Neuroticism constructs are derived from Eysenck and Eysenck concepts [21]. Rigidity is quite similar to construct of Typus melancholicus proposed by Tellenbach [14-17], while Tendency to Isolation and Esoteric Tendency are based on Kretschmer's classical study on relationships between constitution and personality [22]. Frustration tolerance refers to resiliency or stress coping strategy.

Along with MPT the Toronto Alexithymia Scale (TAS-26) [23, 24] was explored for assessment of alexithymia. This scale consists of 26 items, and each item can be scored in points from 1 to 5. The global alexithymia score in TAS-26 may be expressed from 26 to 130 points. All patients whose global TAS-26 score exceeds 74 points were regarded as alexithymic persons. The mean

average of TAS-26 score in nonalexithymic group (N=78) was 58,5+11,5, and in alexithymic group (N=22) was 80,0+4,8 points.

Assessment of psychopathological status of patients has been performed by use Symptom Check List-90 (SCL-90). This questionnaire represents a self-rated scale that has 9 psychiatric symptom groups, consisting of 90 items with a range of five degree severity (0,1,2,3,4). The evaluated psychiatric constructs include somatization, obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideations, and psychoticism [25, 26].

For the assessment of handedness Annet's scale was used [27]. Persons whose global score on that scale was lower than -5 points were regarded as left-handers, whilst persons with global score exceeded +5 points as right-handers. Among all studied patients 73 persons were considered as right-handers (Mean+Std. Dev.: +19,2+6,0) in Annet's score and 31 persons as left-handers (Mean+Std. Dev.: -11,2+10,9).

For analysis purposes all patients were divided into groups in relation to combination of focus lateralization and motor asymmetry (handedness). In line with this rule the next four groups were defined: Left focus/Left-handedness (13 patients), Left focus/Right-handedness (33 patients), Right focus/Left-handedness (17 patients) and Right focus/Right-handedness (36 patients).

3. Statistics

All data were statistically processed by Statistica program (9-th version) on personal computer. On the first step the possible relationship between focus laterality and OCD development was assessed. In addition the mean values of seizure frequency of different semiotics in patients with OCD and in persons without OCD have been calculated. On the next step the mean values of premorbid personality traits, including MPT-constructs and TAS-26 have been calculated, while on the third stage the multiple regression analysis has been performed for OCD construct (SCL-90). Here OCD construct was dependent variable, while the premorbid personality features (TAS-26 χ and MPT constructs) were used as independent variables. On the final stage the values of variances obtained in result of regression analysis were compared between different groups of patients, and the maximal variances were regarded as more robust criteria for prediction of OCD [28].

4. Results

The main results are listed in the next several tables. In Table 1 the mean values of seizure frequency are presented. As can be seen no statistically significant discrepancies between groups with and without OCD are obtained. In other words, the seizure semiotics doesn't determine the OCD development. Noteworthy, the statistically significant relationship between focus laterality and OCD also has not been revealed ($\chi^2=2,25$, $p=0,13$), that implies the lack of influence of focus laterality upon OCD development in patients with epilepsy.

Type of seizure	Patients with OCD (n=19)	Patients without OCD (n=84)	Discrepancy
Primary GTCS	0,05+-0,23	0,27+-0,76	n.s.
Simple partial seizures	25,68+-69,48	49,23+-136,3	n.s.
Sensory simple partial seizures	5,21+-10,11	37,58+-120,67	n.s.
Motor simple partial seizures	20,68+-70,3	14,10+-74,63	n.s.
Complex partial seizures	31,47+-71,44	21,36+-57,71	n.s.
Secondary GTCS	6,89+-13,69	7,20+-12,57	n.s.

Notes: GTCS – Generalized tonic-clonic seizures

Table 1. Mean frequency (per year) of different semiotics seizures in patients with OCD and without OCD in epilepsy

The premorbid personality structure data, quite the contrary, have revealed their role in the origin of OCD, as can be seen from Table 2. As can be seen from table the OCD patients compared with patients without OCD symptoms as a whole, were characterized by less degree of Extraversion and Frustration Tolerance than patients in whom OCD symptoms didn't develop. On the other hand, OCD patients in premorbid personality structure had higher values of Neuroticism, Esoteric Tendencies and Schizoidia in comparison with patients without OCD. The values of Alexithymia, Rigidity and Tendencies to Isolation couldn't discriminate two compared groups of patients.

Personality construct	Patients with OCD (n=19)	Patients without OCD (n=84)	Discrepancy
Extraversion (MPT)	11,74+-5,61	16,38+-5,64	p=0,0016
Neuroticism (MPT)	18,26+-3,69	12,37+-5,44	p=0,000012
Frustration Tolerance (MPT)	5,58+-2,85	8,19+-3,98	p=0,0081
Rigidity (MPT)	12,53+-3,91	13,00+-4,56	n.s.
Tendency to Isolation (MPT)	5,37+-2,65	4,67+-2,50	n.s.
Esoteric Tendencies (MPT)	3,37+-2,29	2,27+-2,08	p=0,044
Schizoidia (MPT)	8,89+-3,59	6,93+-3,72	p=0,039
Alexithymia (TAS-26)	68,94+-13,69	62,35+-13,66	n.s.

Table 2. Mean values of different Munich Personality Test constructs and alexithymia in patients with OCD and without OCD in epilepsy

Based on these obtained data preliminary conclusion can be made that interaction of multifarious personality factors seems to be significant for the OCD origin. In order to reveal such interaction the multiple regression analysis (forward model) has been performed in different groups of patients formed on the basis of different combinations motor lateralization and focus laterality. In other words, this analysis has been performed for prediction of OCD level based on premorbid personality variables.

Main results of that analysis are listed in the Table 3.

Group	Alexithymia	Extraversion	Neuroticism	Frustration tolerance	Rigidity	Tend.to isolation	Esoteric tendency	Schizoidia	R2
All persons (N=99)	-	-0,24	0,48	-	-	-	-	-	0,49
RH (n=69)	-	-0,25	0,55	-	-	-0,25	-	-	0,56
LH (n=30)	0,51	-	-	-	-	-	-	-	0,50
RF (n=53)	-	-0,23	0,62	-	-	-0,35	-	-	0,69
LF (n=46)	-	-	-	-	-	-	-	-	0,35
RHRF (n=36)	-	-0,35	0,67	-	-	-0,27	-	-	0,74
RHLF (n=33)	-0,41	-	0,41	-0,37	-	-	-	-	0,51
LHRF (n=17)	0,53	-	0,38	-	-	-	-	-	0,60
LHLF (n=13)	0,145	-0,64	-	-	0,168	0,983	0,79	-0,92	0,78

Notes: RH – right-handers; LH-lefthanders; RF-right focus patients; LF – left focus patients; RHRF-right-handers with right focus; RHLF – right-handers with left focus; LHRF-lefthanders with right focus; LHLF-lefthanders with left focus; R2 – explained variance.

Table 3. Multiple forward stepwise regression analysis for OCD disorder as dependent variable in different groups of patients with epilepsy

As can be seen from Tab 3 in the final predictive score of OCD the several personality variables are important. These variables included mostly such features, as Alexithymia, Extraversion, and Neuroticism. Noteworthy, Alexithymia has been included into regression equation with positive loadings in left-handers and in group of left-handers with right focus activity. It implies the alexithymia to be a risk factor for OCD development strictly in left-handed TLE patients and particularly in left-handed persons with right focus activity. On the other hand, Alexithymia has been included into regression equation with negative loading in group of right-handed patients with left-sided focus epileptic activity. It implies that in such category of patients Alexithymia reduces the final OCD score and by that exerts protective action against its development.

Noteworthy, the Extraversion and Neuroticism scores both have been included into regression within same several combination of handedness and focus laterality, although with opposite loadings. Thus, Extroversion always had negative loading and by that reduced the final OCD score. It concerned as all patients, as especially patients with right focus activity and the right-handed patients and persons with combination of right-handedness and right focus activity. In other words the high Extraversion exerts protective effect on OCD development, while low level of Extraversion (Introversion) determines OCD and right-handed persons with right focus activity are especially vulnerable to it.

Neuroticism, on the contrary had been included into final regression equation with positive loadings and by that determined the OCD development in the same categories of patients. In other words, Extroversion and Neuroticism have an opposite influence on OCD score, and Neuroticism is thought to be a risk factor for OCD development.

On the final stage comparison of mutual variances between dependent and independent variables in regression analysis has been performed (Tab 3). The comparison revealed that maximal values of variances were observed in regression performed for group of patients with right focus activity and especially for group of right-handers with right-sided focus ($R^2=0,74$) and for person with combination of left-handedness and left focus activity ($R^2=0,78$).

Nevertheless, the role of maximal variance value in the last category of patients (left-handers with left focus activity) shouldn't not been exaggerated, since no statistically significant loading for any personality construct has been observed.

Conversely, the minimal values of explained variances were obtained for whole group of patients where handedness and focus laterality have not been taken into account

5. Discussion

The current study is rather the second one, in which the premorbid personality features were evaluated as risk factors in combination with certain neurobiological variables in patients with TLE. Earlier we have performed the similar work on relationships between premorbid personality traits and development of depression and anxiety states in temporal lobe epilepsy [29]. The principal limitations of the current study concern the small size of LHRF and LHLF

groups, that couldn't reveal always statistically significant correlations and discrepancies between compared groups. Nevertheless, obtained data have shown that based on certain so-called premorbid variables rated subjectively by patients themselves the prediction of OCD in TLE patients is quite possible.

Principally, the identification and diagnostics of OCD pathology have been performed by psychiatrists using objective scales, and those physicians were blind to data on patient personality traits. Such approach has been used in order to avoid any bias in the qualification of patient personality structure.

Another reason for the criticism is statement that traits used in study depict not premorbid period in TLE patients at all, but personality changed due epilepsy course itself. Here should be stressed that similar approach has been already widely used in numerous studies on different contingent of patients including organic brain disorders and their authors believe that MPT constructs can assess strictly premorbid personality [15-18]. Moreover, personality changes in TLE patients are characterized as a rule by other kind of features, and viscosity is the prominent trait among them and it isn't included into either construct of MPT. In this context MPT doesn't depict the structure of epileptic personality at all, although Rigidity construct can be seen as similar but not identical to epileptic personality changes.

The principal results of present study have shown, that neither seizure semiotics, nor focus lateralization (assessed separately from personality features) couldn't discriminate epileptic patients in terms of risk OCD development. However, such prediction becomes probable, if take into account the personality traits.

The third reason for critic of current study may concern the fact that here has not been used Yale-Brown scale. Here should be stressed that OCD construct included in SCL-90 questionnaire describes thoroughly obsessive-compulsive symptoms and may be adequately enough used for the assessment of such signs severity along with other psychopathological constructs [25, 26].

The main results of the current study have shown that premorbid personality features have multifactorial influence on OCD development in patients with TLE. Thus, obsessionality in patients with TLE may evolve similarly from such different personality traits as alexithymia, low extraversion score (introversion) and neuroticism and esoteric tendencies. Nonetheless, the certain premorbid personality trait becomes relevant for OCD development strictly on condition that some definite neurobiological variables, such as handedness, focus lateralization and their combination in TLE patients should also be taken into account. Moreover, the certain interaction among concrete personality characteristics with definite neurobiological variables indeed exists.

Thus, Alexithymia may become risk factor for OCD appearance strictly in left-handed patients and in left-handed persons with right focus activity. Quite the contrary, Alexithymia may play protective role against OCD development in right-handed patients with left focus activity. In other words, quite mirror image role of Alexithymia for OCD origin in epilepsy depends on interaction between handedness and focus lateralization.

Neuroticism and Extroversion, on the other hand, were risk factors for OCD in cases of right-handed patients with right-focus activity, although Neuroticism had positive loading for OCD

development in right-handed patients with the left focus activity too. Obviously, the right-handedness seems to be more important for Neuroticism construct in terms of its role in OCD triggering than focus laterality. It implies that Neuroticism as personality feature may be maximally expressed in the right-handed, but not in the left-handed persons, i.e. seems to be the prerogative of persons with normal motor lateralization.

Obtained results have confirmed data of our previous work, that Alexithymic and Neurotic traits are thought to depict the different types of personality that rather exclude each other. In this context the appearance of similar OCD disorders in TLE patients with such different personality structures seems to be unexpected and rather contradictory and should be properly explained. Unfortunately, only speculative explanation may be proposed in this context. Obviously, the OCD and affective and anxiety disorders seem to be the adaptive forms of reaction on environmental and internal factors, and could appear in evolution of animals and *Homo sapiens*. As adaptive forms of behavior these disorders are required in persons with different types of neurobiological mechanisms, including motor lateralization and focus laterality in TLE.

Contrary to our initial expectations we couldn't find any significant effect of construct "Rigidity" on OCD in patients with TLE, although the repetition of obsessions seems to be an attribute of rigidity. Principally, in our previous work we couldn't find any relationship between Rigidity and depression development in patients with epilepsy [29]. It implies that "Status melancholicus" concept is not rather relevant enough for prediction of affective disorders and OCD development, and mentioned psychiatric co-morbidity have different personality predisposition traits that become trigger risk factors in TLE. Obviously, that alexithymia, extraversion, neuroticism and esoteric tendencies are more relevant for depression, anxiety and OCD in persons with TLE, than Rigidity.

Based on the data obtained in the current and previous work [29] conclusion can be made, that premorbid personality profile of affective, anxiety disorders and OCD is quite similar and includes high Neuroticism level and low Extraversion (high Introversion) level in the right-handed patients with right focus activity. Besides, the high level of Alexithymia seems to be *Conditio sine qua non* for the OCD and depression and anxiety in left-handed persons. Obviously that Neuroticism combined with low level of Extraversion (Introversion), on one side, and Alexithymia, on the other side, may cause the similar psychopathological disorders such as OCD and depression and anxiety states in patients with different neurobiological predisposition. It implies that Neuroticism, Extraversion and Alexithymia represent the universal personality constructs for development as affective, as OCD. Further studies are required to elucidate the pathogenic mechanisms of co-morbid psychopathology in person with epilepsy.

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