

## The influence of clinical and immune variables on psychopathological syndromes in partial epilepsies in relation to handedness

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### SUMMARY

**Background.** The role of neurobiological and immunity variables in the genesis of psychopathological syndromes in patients with partial epilepsy is not properly understood. It concerns also the role of handedness.

**Aim.** The study was carried out in order to find the influence of clinical (neurobiological) and immune variables on co-morbid psychopathological syndromes in patients with epilepsy separately for right-handers and left-handers.

**Material and Methods.** Ninety two (92) patients with epilepsy were recruited into the study. Among the studied patients were 85 right-handers and 7 left-handers. The data on frequency of each seizure semiotics, the assessment of seizures severity and the length of remission were used as main basic clinical variables. Assessment of psychopathological status of patients has been performed by using of Symptom Check List-90 (SCL-90). The amounts of different lymphocytes clusters also were calculated. The product moment correlation analysis was used to find the possible relationships separately for right-handers and left-handers.

**Results.** In the right-handers group only significant correlation between the focal motor seizure frequency and value of Hostility construct of SCL-90 scale ( $r=0.284$ ,  $p=0.045$ ), and between the total count of T-lymphocytes and expression of Psychoticism, SCL-90 ( $r=-0.271$ ,  $p=0.049$ ). In the left-handers group stochastically significant correlations between focal seizures with impaired awareness (FSIA), focal to bilateral tonic-clonic seizures (FBTCS) and National Hospital Seizure Severity Scale (NHS3) score with 5 SCL-90 constructs were revealed. The regulatory index (CD4/CD8 ratio) correlates positively with Obsessions ( $r=0.780$ ,  $p=0.039$ ); Interpersonal sensitivity ( $r=0.80$ ,  $p=0.031$ ); Depression ( $r=0.834$ ,  $p=0.02$ ); Aggression ( $r=0.926$ ,  $p=0.003$ ); Paranoid ideations ( $r=0.873$ ,  $p=0.01$ ) and Psychoticism ( $r=0.913$ ,  $p=0.004$ ).

**Conclusion.** Neurobiological and immune variables determine the psychopathological constructs strictly in left-handers.

**Key words:** epilepsy • seizure frequency • immunity variables • psychopathological constructs

## BACKGROUND

Epilepsy represents neurological disease with a broad palette of concomitant psychopathological disorders. These disorders cause additional issues in the life of patients with epilepsy and make worse their social and clinical prognosis.

The range of psychopathological disorders spreads from affective disorders, including depression and anxiety, to severe psychosis and mental deterioration that demands the precise and rapid diagnostics and adequate treatment.

At present several possible mechanisms which could explain the appearance of concomitant psychopathology in epilepsy have been proposed. In this context some authors believe that temporal lobe epilepsy especially with left hemisphere focus and concomitant reduced function of frontal lobes (so-called hypofrontality) and focal seizures with impaired awareness (FSIA) belongs to the main risk factors of co-morbid psychopathological disorders and depression in particular (Mendez et al., 1986, 1994; Altshuler et al., 1990; Blumer, 1992; Perini et al., 1996; Schmitz, 2002, 2005; Attarian et al., 2003; Kanner, 2005).

Nevertheless, such pure neurobiological approach could not explain the specific nature of different psychopathological disorders in epilepsy and should not be regarded as a universal one. In other words, why is it that in some cases depression and anxiety occurs, while in other cases psychosis or obsessive-compulsive disorder can occur and is not properly understood.

Clearly, there are other possible mechanisms that may contribute to the development of psychopathology in epilepsy, and the immune system may be responsible for such role, since the psychoneuroimmunological interrelationship at present is regarded as a principal factor in the pathogenesis of depressions, anxiety and psychoses. Nevertheless, the exact specific mechanisms which could explain the involvement of immunity in the pathogenesis of psychopathology are not known (Ader, 1980; Birnbaum, 1998; Daruna, 2004; Vedhara, Irwin, 2005).

In our previous studies the role of immunity mechanisms in the pathogenesis of partial forms of epilepsy has been reported (Kalinin et al., 2016; Kalinin et al., 2018). It concerned the influence of a combination of immunity variables with focus lateralization, gender and handedness on the frequency of focal sensory seizures (FSS) in epilepsy. Thus, the highest frequencies of FSS were revealed in the cases of low CD4/CD8 ra-

tio combined with left temporal focus, female gender and left-handedness. On the other hand, the maximal frequency of FSS was revealed in the patients with left frontal focus combined with high B-lymphocyte level. The more severe seizures were revealed in left-handers with low CD8 and high CD4/CD8 ratio and in frontal left focus and high T-lymphocyte level. There was a correlation between CD4 cell level and length of remission (Kalinin et al., 2016).

To-date, the role of immunity variables in the genesis of co-morbid psychopathological symptoms and syndromes has not been properly studied yet. It concerns also the role of handedness (motor asymmetry) in epilepsy.

It should be emphasized that handedness per se is not important for the development of psychopathology and immunity functions, but underlying cerebral structure and functions that determine the handedness can influence the psychopathology and immunity in epilepsy.

Thus, to illustrate the relationship between the handedness and language dominance, the data by Knecht et al. (2000) may be cited. According to these data the incidence of right hemisphere language dominance increases linearly with degree of left-handedness from 4% in strong right-handers to 27% in strong left-handers (Knecht et al., 2000).

Obviously, the structural and functional cerebral organization in the right- and the left-handers is different, and by that may differently determine their psychopathology (Geschwind, Behan, 1982; Geschwind, Galaburda, 1985a; 1985b).

On the other hand, according to the model proposed by Geschwind and Behan, (1982) and Geschwind and Galaburda (1985a; 1985b) there is a close relationships between handedness and immune mechanisms. The authors stressed the fact that there is a higher frequency of auto-immune disorders in left-handers compared with the right-handers. Based on these data the conclusion can be made that higher immunity tension seems to be a requisite of patients with anomalous cerebral lateralization that, in turn, can lead to specific psychopathology distinct from symptoms of right-handers.

In one of our previous studies the role of cerebral lateralization in the origin of some psychopathological syndromes and intelligence deficiency in patients with epilepsy has been confirmed, although the state of immunity mechanisms in this context has not been studied yet (Kalinin et al., 2010; Kalinin et al., 2014).

## AIM

The current pilot study has been designed and performed in order to find the possible influence of cellular immune and neurobiological variables (frequencies of seizures of different semiotics and their severity) on co-morbid psychopathology in relation to handedness in patients with partial forms of epilepsy.

## MATERIAL AND METHODS

This study enrolled 92 patients with epilepsy. All patients attended the Department of Brain Organic Disorders and Epilepsy of Moscow Research Institute of Psychiatry.

The patients comprised 38 men and 54 women. The diagnosis of symptomatic epilepsy was set in 40 patients, the diagnosis of cryptogenic form – in 52 patients. Temporal-lobe epilepsy was diagnosed in 36 patients, the frontal-lobe epilepsy – in 16 patients and temporal-frontal epilepsy – in 40 patients. All patients were scanned through magnetic resonance (MRI). No any visible pathology (hippocampal sclerosis or limbic pathologies) could be found in the left-hander and right-hander groups.

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 32 patients, the right-sided foci – in 30 patients, and bilateral foci – in 30 patients.

The data on frequency of each seizure semiotics and the length of remission were collected from patient diaries. In this context the mean number of each seizure type per month has been calculated for the last 6 months and the length of remission (the full control over seizures) in the months preceding the admittance to hospital has been included into statistical analysis.

The new operational classification of seizure types by the International League Against Epilepsy has been used in the current study (Fisher et al., 2017).

Along with these data, the assessment of seizures severity according to the National Hospital Seizure Severity Scale (NHS3) (O'Donoghue et al., 1996) has been performed.

Assessment of psychopathological status of patients has been performed by using the 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 (Derogatis et al., 1973; Derogatis, Cleary, 1977). This scale is widely used in psychiatry and its validity has been proven in many studies, and particularly in our trials (Kalinin et al., 2010; Kalinin et al., 2013).

In addition, the assessment of handedness Annett's scale was used (Annett, 1970). Patients, whose global score on that scale was lower than – 5 points were regarded as left-handers, while patients with global score exceeded +5 points – as right-handers. Among the studied patients, 85 patients were considered as right-handers (Mean  $\pm$  Std. Dev.: +21.9  $\pm$  2.7) in Annett's score and 7 persons as left-handers (Mean  $\pm$  Std. Dev.: –9.9  $\pm$  12.9).

The so-called pathological left-handedness has not been observed in our studied group. All patients were scanned through MRI and any visible pathology (hippocampal sclerosis or limbic pathologies) has not been observed in the left-hander group.

The blood samples for immune system testing were taken in every patient after he or she had been admitted to hospital. The analyses have been performed on cytofluorimeter FC 500 (Beckman Coulter).

The amount of different lymphocytes clusters were calculated. Among them the number of T-lymphocytes (CD3+), T-helpers (CD3+CD4+), T-cytotoxic (CD3+CD8+), T-NK (CD3+CD16+CD56+), B-lymphocytes (CD3+CD19+), Natural Killers (CD3-CD16+CD56) and regulatory index (CD4/CD8 ratio) were analyzed.

## Statistics

In order to find any possible relationships between neurobiological and immunity variables on the one hand, and SCL-90 constructs on the other hand, the Spearman rank correlation analysis has been performed separately within left-handers group and right-handers group (Feinstein, 2002; Mathews, Farewell, 2007).

That method is usually used in order to find a probable relationship between two or more groups of quantitative variables, where the form of distribution is not normal and results in "r" – a correlation coefficient, that may vary from –1 (the strong inverse relationship) to +1 (the strong positive relationship) (Feinstein, 2002; Mathews, Farewell, 2007).

Comparison of means of neurobiological, immunological and psychopathological variables between right-handers and left-handers was undertaken by using the Student's test.

## RESULTS

The results are shown in tables 1–6. In table 1 the comparison of means of neurobiological, immunological and psychopathological variables between right-handers and left-handers has been undertaken. As can be seen the left-handers were characterized by much more high frequencies of two types of seizures compared with right-handers. These seizures include focal seizures (FS) and focal sensory seizures (FSS). These discrepancies imply that left-handers, as a rule, have much worse prognosis in terms of frequencies of mentioned seizures, although the mechanisms of such discrepancies remain unknown.

Data on comparison of psychopathological data (SCL-90 constructs) are included in table 2. The only significant discrepancy was revealed for sensitivity construct, and left-handers have less sensitivity level compared with right-handers ( $4.71 \pm 2.43$  vs  $8.06 \pm 6.85$ ;  $p = 0.018$ ).

Tables 3 and 4 include the values of Spearman correlations coefficient between frequency of seizures and SCL-90 constructs in group of right-handers (Tab. 3) and left-handers (Tab. 4). As can be seen the right-handers were characterized only by one significant correlation between the focal motor seizure (FMS) frequen-

**Table 1.** Comparison of mean values of seizure frequency of different semiotics and immune variables in groups of left-handers and right-handers

Variable	Left-handers	Right-handers	Significance
Focal seizures (FS)	154.71 ± 272.51	18.41 ± 46.91	<b>p = 0.000</b>
Focal sensory seizures (FSS)	150.00 ± 275.38	15.44 ± 45.72	<b>p = 0.000</b>
Focal motor seizures (FMS)	11.86 ± 20.55	7.66 ± 40.21	n.s.
Focal seizures with impaired awareness (FSIA)	8.71 ± 22.62	14.65 ± 36.86	n.s.
Focal to bilateral tonic-clonic seizures (FBTCS)	9.57 ± 17.48	14.98 ± 22.39	n.s.
NHS3	16.71 ± 12.78	13.15 ± 8.67	n.s.
T-lymphocytes	77.63 ± 5.19	73.97 ± 6.60	n.s.
T-helpers CD3+CD4	46.59 ± 8.94	46.59 ± 6.71	n.s.
T-cytotoxic (CD3+CD8+)	28.87 ± 7.51	25.62 ± 6.22	n.s.
T-NK (CD3+CD16+CD56+)	9.29 ± 5.91	6.01 ± 4.16	n.s.
B-lymphocytes (CD3+CD19+)	10.24 ± 3.02	12.62 ± 4.97	n.s.
Natural Killers (CD3-CD16+CD+56)	9.81 ± 3.20	11.69 ± 5.69	n.s.
Regulatory index (CD4/CD8) ratio	1.79 ± 0.79	1.97 ± 0.65	n.s.

Note: statistically significant discrepancies are marked in bold.

**Table 2.** Comparison of psychopathological variables in patients with left-handedness and right-handedness

Variable	Left-handed Patients (N = 7)	Right-handed Patients (N = 59)	Significance
Somatization SCL-90)	5.57 ± 3.69	7.15 ± 6.18	N.S.
Obsession (SCL-90)	6.14 ± 4.45	8.34 ± 6.47	N.S.
Sensitivity (SCL-90)	<b>4.71 ± 2.43</b>	<b>8.06 ± 6.85</b>	<b>p = 0.018</b>
Depression (SCL-90)	6.14 ± 5.55	9.47 ± 8.68	N.S.
Anxiety (SCL-90)	5.00 ± 2.65	5.59 ± 6.01	N.S.
Aggression (SCL-90)	2.86 ± 2.67	5.14 ± 4.33	N.S.
Phobia (SCL-90)	1.43 ± 2.07	3.45 ± 3.98	N.S.
Paranoid (SCL-90)	3.00 ± 3.06	4.00 ± 3.80	N.S.
Psychoticism (SCL-90)	2.57 ± 2.64	3.40 ± 4.30	N.S.
Total Score (SCL-90)	37.43 ± 23.96	46.47 ± 31.47	N.S.

Note: Statistically significant discrepancies are marked in bold.

**Table 3.** The rank Spearman correlations between frequency of seizures of different semiotics and SCL-90 constructs in group of right-handers

Variable	Focal seizures (FS)	Focal sensory seizures (FSS)	Focal motor seizures (FMS)	Focal seizures with impaired awareness (FSIA)	Focal to bilateral tonic-clonic seizures (FBTCS)	NHS3
Somatization (SCL-90)	-0.029	-0.111	-0.044	0.000	-0.039	0.137
Obsession (SCL-90)	-0.024	-0.035	0.031	0.065	-0.112	0.069
Interpersonal sensitivity (SCL-90)	0.025	-0.004	0.042	0.164	-0.064	0.150
Depression (SCL-90)	0.065	0.057	0.106	-0.023	-0.043	-0.016
Anxiety (SCL-90)	-0.027	-0.043	0.004	0.010	-0.147	0.169
Hostility (SCL-90)	0.138	0.196	<b>0.284</b> <b>p=0.045</b>	0.007	0.016	0.082
Phobic anxiety (SCL-90)	-0.160	-0.144	-0.128	-0.077	-0.128	-0.069
Paranoid ideations (SCL-90)	-0.086	-0.071	0.000	0.087	-0.064	0.119
Psychoticism (SCL-90)	-0.107	-0.126	-0.047	-0.028	-0.088	0.086

Note: Statistically significant coefficients are marked in bold.

**Table 4.** The rank Spearman correlations between frequency of seizures of different semiotics and SCL-90 constructs in group of left-handers

Variable	Focal seizures (FS)	Focal sensory seizures (FSS)	Focal motor seizures (FMS)	Focal seizures with impaired awareness (FSIA)	Focal to bilateral tonic-clonic seizures (FBTCS)	NHS3
Somatization (SCL-90)	0.069	0.074	-0.350	0.406	0.444	0.669
Obsession (SCL-90)	-0.110	-0.116	-0.093	<b>0.876</b> <b>p=0.01</b>	<b>0.875</b> <b>p=0.01</b>	0.651
Interpersonal sensitivity (SCL-90)	-0.708	-0.710	0.733	0.426	0.444	0.620
Depression (SCL-90)	-0.403	-0.398	0.158	<b>0.947</b> <b>p=0.001</b>	<b>0.913</b> <b>p=0.004</b>	<b>0.823</b> <b>p=0.023</b>
Anxiety (SCL-90)	-0.071	-0.080	-0.015	<b>0.833</b> <b>p=0.02</b>	<b>0.915</b> <b>p=0.004</b>	<b>0.769</b> <b>p=0.043</b>
Aggression (SCL-90)	-0.528	-0.521	0.024	0.686	0.616	0.662
Phobic anxiety (SCL-90)	-0.337	-0.336	-0.041	<b>0.975</b> <b>p=0.000</b>	<b>0.973</b> <b>p=0.000</b>	<b>0.762</b> <b>p=0.047</b>
Paranoid ideations (SCL-90)	-0.412	-0.416	0.287	<b>0.871</b> <b>p=0.011</b>	<b>0.899</b> <b>p=0.006</b>	<b>0.858</b> <b>p=0.013</b>
Psychoticism (SCL-90)	-0.470	-0.459	0.356	0.749	0.690	<b>0.847</b> <b>p=0.016</b>

Note: Statistically significant coefficients are marked in bold.

cy and value of Hostility construct of SCL-90 scale ( $r = 0.284$ ,  $p = 0.045$ ), while in the other cases there was no significant correlations between the seizure frequencies and SCL-90 constructs.

In contrast, in the group of left-handers much more stochastically significant correlations between focal seizures with impaired awareness (FSIA), focal to bilateral tonic-clonic seizures (FBTCS) and NHS3 score with 5 SCL-90 constructs were revealed. Thus, both these

seizure frequencies correlated positively with obsession ( $r = 0.876$ ,  $p = 0.001$ ;  $r = 0.875$ ,  $p = 0.001$  respectively); with depression ( $r = 0.947$ ,  $p = 0.001$ ;  $r = 0.913$ ,  $p = 0.004$ ); with anxiety ( $r = 0.833$ ,  $p = 0.02$ ;  $r = 0.915$ ,  $p = 0.004$ ); with phobic anxiety ( $r = 0.975$ ,  $p = 0.000$ ;  $r = 0.973$ ,  $p = 0.000$ ) and with paranoid construct ( $r = 0.871$ ,  $p = 0.011$ ;  $r = 0.899$ ,  $p = 0.006$ ).

Similarly, NHS3 correlated positively with depression ( $r = 0.823$ ,  $p = 0.023$ ); anxiety ( $r = 0.769$ ,  $p = 0.043$ );

**Table 5.** The rank Spearman correlations between immune variables and SCL-90 constructs in group of right-handers

Variable	T-lymph.	CD3+CD4+	CD3+CD8+	T-NK	B-lymph.	NK	CD4/CD8 ratio
Somatization (SCL-90)	-0.209	-0.089	-0.109	-0.063	-0.020	0.169	0.040
Obsessions (SCL-90)	-0.228	0.000	-0.232	-0.078	-0.010	0.175	0.182
Interpersonal sensitivity (SCL-90)	-0.169	-0.006	-0.141	-0.105	-0.090	0.173	0.145
Depression (SCL-90)	-0.169	-0.045	-0.108	-0.159	-0.023	0.123	0.085
Anxiety (SCL-90)	-0.172	-0.112	-0.023	-0.153	-0.026	0.124	-0.023
Aggression (SCL-90)	-0.119	0.074	-0.184	-0.202	0.063	0.061	0.195
Phobic anxiety (SCL-90)	-0.043	0.095	-0.188	-0.211	0.006	-0.027	0.187
Paranoid ideations (SCL-90)	-0.208	-0.006	-0.187	-0.058	-0.070	0.185	0.154
Psychoticism (SCL-90)	<b>-0.271</b> <b>p=0.05</b>	-0.043	-0.199	-0.213	-0.021	0.244	0.104

Note: Statistically significant coefficients are marked in bold.

**Table 6.** The rank Spearman correlations between immune variables and SCL-90 constructs in group of left-handers

Variable	T-lymph.	CD3+CD4+	CD3+CD8+	T-NK	B-lymph.	NK	CD4/CD8 ratio
Somatization (SCL-90)	-0.612	-0.099	-0.291	-0.313	<b>0.942</b> <b>p=0.002</b>	-0.122	0.209
Obsessions (SCL-90)	-0.128	0.529	-0.735	-0.424	0.107	0.218	<b>0.780</b> <b>p=0.039</b>
Interpersonal sensitivity (SCL-90)	0.249	<b>0.822</b> <b>p=0.023</b>	<b>-0.763</b> <b>p=0.046</b>	-0.032	-0.152	-0.133	<b>0.800</b> <b>p=0.031</b>
Depression (SCL-90)	-0.307	0.493	<b>-0.796</b> <b>p=0.032</b>	-0.409	0.417	0.088	<b>0.834</b> <b>p=0.020</b>
Anxiety (SCL-90)	-0.241	0.197	-0.429	-0.109	0.496	-0.144	<b>0.470</b>
Aggression (SCL-90)	-0.303	0.637	<b>-0.954</b> <b>p=0.001</b>	-0.515	0.115	0.432	<b>0.925</b> <b>p=0.003</b>
Phobic anxiety (SCL-90)	-0.433	0.241	-0.625	-0.262	0.441	0.194	<b>0.657</b>
Paranoid ideations (SCL-90)	-0.074	0.659	<b>-0.829</b> <b>p=0.021</b>	-0.265	0.218	-0.023	<b>0.873</b> <b>p=0.010</b>
Psychoticism (SCL-90)	-0.207	0.682	<b>-0.897</b> <b>p=0.006</b>	-0.518	0.459	0.074	<b>0.913</b> <b>p=0.004</b>

Note: Statistically significant coefficients are marked in bold.

phobic anxiety ( $r = 0.762$ ,  $p = 0.047$ ); paranoid thoughts ( $r = 0.858$ ,  $p = 0.013$ ) and psychoticism ( $r = 0.847$ ,  $p = 0.016$ ).

It implies that in the group of left-handers the high frequencies of FSIA, FBTCS and NHS3 score determine the high level of all mentioned SCL-90 constructs.

Tables 5 and 6 include the results of correlation analy-

sis between immunity variables and SCL-90 constructs separately for group of the right-handers (Tab. 5) and the left-handers (Tab. 6).

As can be seen in the group of right-handers only one stochastically significant and inverse correlation exists between the total count of T-lymphocytes and ex-

pression of Psychoticism, SCL-90 ( $r = -0.271$ ,  $p = 0.05$ ). It implies that an increase in count of T-lymphocytes is related to reduction of Psychoticism level, although the role of this relationship should not be exaggerated due the small size of correlation.

In contrast, in the group of left-handers a much more statistically significant correlations of high value was observed despite the small size of group (Tab. 6).

Thus, the regulatory index (CD4/CD8 ratio) correlates positively with obsessions ( $r = 0.780$ ,  $p = 0.039$ ); interpersonal sensitivity ( $r = 0.80$ ,  $p = 0.031$ ); depression ( $r = 0.834$ ,  $p = 0.02$ ); aggression ( $r = 0.926$ ,  $p = 0.003$ ); paranoid ideations ( $r = 0.873$ ,  $p = 0.01$ ) and psychoticism ( $r = 0.913$ ,  $p = 0.004$ ). It implies, that high immunity tension relates to high expression of all mentioned variables and determines the unspecific polymorphic psychopathological syndrome in left-handers with epilepsy.

In line with the obtained findings are also data on inverse correlations between CD3+CD8+ cell count and interpersonal sensitivity ( $r = -0.763$ ,  $p = 0.046$ ); depression ( $r = -0.796$ ,  $p = 0.032$ ); aggression ( $r = -0.954$ ,  $p = 0.001$ ); paranoid ideations ( $r = -0.829$ ,  $p = 0.021$ ) and psychoticism ( $r = -0.897$ ,  $p = 0.006$ ). These findings again confirm the role of immunity tension in the origin of polymorphic psychopathological syndromes in left-handers with epilepsy.

On the other hand, in the left-handers the count of B-lymphocytes (CD3+CD19+) positively correlated with somatization (SCL-90) ( $r = 0.942$ ,  $p = 0.002$ ). Once again the high level of correlation, reaching the so-called functional relationship has been obtained.

## DISCUSSION

The present study may be criticized for the unequal size of compared groups and too small left-handers' group. Here must be stressed that frequency of left-handedness in a general population usually reaches near 8–11% (Hardyck, Petrinovich, 1977; Brackenbridge, 1981; Raymond et al., 1996; Mc Manus, 2009) and our findings are in full accordance with these data.

Obtained results have shown that left-handers with epilepsy are characterized by much more frequencies of FS and FSS. In other words, the cerebral organization of left-handed patients with epilepsy predisposes to development of more frequent FS and FSS. Nonetheless, the exact mechanisms of such influence on seizures frequencies remain unknown.

Here should be stressed, that despite such discrepancies neither FS nor FSS frequencies correlated with

SCL-90 constructs and consequently could not influence psychopathology. On the other hand, focal seizures with impaired awareness (FSIA) and focal to bilateral tonic-clonic seizures (FBTCS) have no significant discrepancies between right-handers and left-handers, but both significantly correlate with SCL-90 constructs. It implies that only these seizures can determine the psychopathology in left-handed patients although the FSIA and FBTCS frequencies have no significant discrepancies between left-handers and right-handers.

Principally that despite the small sample of studied left-handers the statistically significant correlation between frequency of seizures and psychopathological constructs on the one hand, and between immunity variables and psychopathological constructs of SCL-90, on the other hand, have been observed.

Moreover, the values of observed correlations in the left-handers group reached near 1.0 that implies the strong and practically functional connections between mentioned above variables.

Comparison of right-handers and left-handers did not reveal any discrepancies between groups in frequency of seizures of different semiotics and immunity variables.

Nevertheless, only one construct of SCL-90 (Interpersonal sensitivity) revealed statistically significant discrepancy, and the mean value of that item was higher in the group of right-handers ( $8.06 \pm 6.85$  vs  $4.71 \pm 2.43$ ;  $p = 0.018$ ) It implies that right-handers usually are more sensitive compared with left-handers, while the latter are much more resistant to interpersonal relationships.

The principal results of the current study have shown that right-handers and left-handers with epilepsy have discrepancies in terms of interaction between seizure frequencies, their severity and co-morbid psychopathological variables on one hand, and between immunity variables and psychopathological constructs, on the other hand.

Thus, in right-handers the psychopathological syndromes are practically independent from the mentioned above variables, while in the left-handers there are strong positive correlations between seizure frequencies, their severity, immunity variables and psychopathological constructs.

In other words, the studied neurobiological and immune variables determine the psychopathological structure of co-morbid disorder strictly in left-handers.

It should be stressed, that immunity variables were quite comparable in groups of left- and right-handers.

It means that immunity tension as a whole does not depend on handedness. In this context our data contradict the hypothesis of Geschwind, Behan (1982) and Geschwind, Galaburda (1985a, 1985b) about higher risk of immune pathology, including auto-immune disorders in patients with left-handedness. Nevertheless, not all studies have confirm this hypothesis (McKeever, Riche, 1990; Bryden et al., 1994; Bryden et al., 2005). In the first study the Laterality quotients from the Edinburgh Handedness Inventory were unrelated to immune disorders in both sexes. The authors conclude, that based on these data the Geschwind-Behan-Galaburda model about linkage between left-handedness and immune pathology could not be confirmed (McKeever, Riche, 1990; Bryden et al., 1994; Bryden et al., 2005).

Nevertheless, the strong linkage between immunity and psychopathology and between seizure frequency and psychopathology seems to be the prerogative of left-handedness, but not of right-handedness in epilepsy.

Thus, in left-handers the high frequency of FSIA, FBTCS and NHS3 score resulted in the more severe syndromes of obsessions, depression, anxiety, phobic anxiety and paranoid ideations. In other words, in such cases the more severe conglomerate of affective, anxiety and paranoid syndromes can appear in comparison with right-handers.

Similarly, the high level of regulatory index (CD4/CD8 ratio) depicts the high level of immunity tension and low level of CD3+CD8+ cells corresponds to it, and all that determines the more severe level of psychotic and affective symptoms with aggression, paranoid thoughts and psychoticism strictly in left-hander, but not in right-hander patients with epilepsy.

## CONCLUSION

The principal conclusion from the present study concerns the fact, that prediction of co-morbid psychopathological syndromes in patients with epilepsy is quite possible based upon the clinical and immunity data strictly in patients with left-handedness, but not in right-handedness.

The exact mechanism of such discrepancies between right-handers and left-handers with epilepsy are not known and should be elucidated in the future studies.

## CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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