

SOME QEEG PARAMETERS AND GENDER DIFFERENCES IN SCHIZOPHRENIA PATIENTS

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SUMMARY

Background: Gender issues are extensively explored in schizophrenia. A mounting body of research evidence suggests that there are gender differences in the age at onset, duration of untreated psychosis and presented psychopathology. In recent years, in order to obtain neurophysiologic explanation for the disturbed behavior and thinking in schizophrenia, numerous studies have been performed focusing on the QEEG parameters. However, the results were inconclusive. The aim of this study was to investigate the gender differences in some clinical and QEEG parameters in schizophrenia patients.

Subjects and methods: Thirty schizophrenia patients were enrolled in the study (M/F ratio 13/17; mean age 34 years). The QEEG parameters which were analyzed were amplitude, mean frequency and relative power of the main bands of the basic activity. Clinical assessment was performed using the PANSS, BPRS and CGI scales.

Results: QEEG parameters demonstrating statistically significant difference were amplitude and relative power in beta activity and lower mean theta frequency over left frontal, temporal and parietal regions in female patients who also had statistically significant differences in PANSS and BPRS scores.

Conclusion: Differences in amplitude and relative power in the beta bands in female schizophrenic patients are associated with more severe actual psychopathology. Considering the relatively small sample, the current results must be replicated with a larger group of drug-free patients to confirm the findings.

Key words: schizophrenia – gender – QEEG - PANSS

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INTRODUCTION

Gender issues are extensively explored in schizophrenia because they can not be affected by the disorder. In the last decade there have been numerous studies examining the contribution of sex differences to the heterogeneity of schizophrenia phenomenology (Tammimga 1997, Seeman 2004), some of them transcultural (Thomas et al. 2010). The majority of investigations have been focused on gender differences in the epidemiology and clinical expression of schizophrenia. Several studies found differences in the onset of schizophrenia in younger male patients (Angermeyer et al. 1990, Leung & Chue 2000, Moriarty et al. 2001) whereas some studies found that female patients tend to have better short and middle-term course (Usall et al. 2003) and less bizarre delusions (Angermeyer et al. 1990). On the other hand male schizophrenic patients tend to present negative symptoms, less severe positive symptoms and poorer functional outcome (Taylor & Langdon 2006). According to some investigators the range of the duration of untreated psychosis varies greatly and the duration of untreated psychosis could lead to the presence of negative symptoms and poor outcome (Norman et al. 2005), but others have not found this relationship (Keshavan et al. 2003). In addition, a sex difference in the functional brain connectivity has been examined by other researchers (Slewa-Younan et al. 2004).

Measurement of the presented psychopathology was usually performed with several clinical scales such as the Brief Psychiatric Rating Scale (BPRS), or the Clinical Global Impression (CGI) scale (Mortimer 2007). However, in an attempt to provide more comprehensive assessment of the symptoms of schizophrenia in clinical and research settings the Positive and Negative Syndrome Scale (PANSS) for schizophrenia was developed (Kay et al. 1987) and is regarded as a reliable means of symptom assessment (Mass et al. 2000).

In order to obtain neurophysiologic explanation for the disturbed behavior and thinking in schizophrenia other investigations actual in the recent years were performed focusing on the QEEG parameters in schizophrenia (John et al. 1994, Begić et al. 2000, Harris et al. 2001, John et al. 2009). Research on QEEG activity (power spectra, relative power, amplitude, mean frequency in the different bands) has shown intriguing results in patients with schizophrenia. Most of the studies reported that patients with schizophrenia have increased beta and slow frequency powers (Begić et al. 2011) and reduced alpha power, and amongst them were the results from our previous investigation (Manuševa et al. 2009). Other studies showed no differences, even opposite results have been reported (Gerez & Tello 1995). In recent studies different symptom clusters have been correlated to QEEG frequency bands (Gross et al. 2006). Some authors think that EEG abnormalities are associated with schizophrenia and reflect non-genetic,

pathological developments of the brain (Stassen et al. 1999) or that disruption of frontal-temporal connectivity appears to have a specific relationship to psychomotor poverty in schizophrenia (Gross et al. 2006).

The aim of this study was to investigate the gender differences in QEEG parameters (amplitude, mean frequency and relative power), the age at onset, duration of the disease and the presented psychopathology in schizophrenia patients.

SUBJECTS AND METHODS

Subjects

The study recruited thirty (13 male and 17 female) inpatients from the University Psychiatry Clinic. All patients fulfilled the ICD-10 diagnostic criteria for schizophrenia and were drug-free or without anti-psychotic therapy at least two days before the QEEG recording in order to avoid immediate drug effects. Subjects with a history of neurological disorders, chronic medical disease, alcohol or drug abuse and mental retardation were excluded.

Methods

Complete medical history and clinical examination were performed in the evaluation of the participants. The patients' global psychopathology was evaluated with the PANSS scale and in the present study we used the following components: positive subscale, negative subscale and total score. For the evaluation of the severity of the disorder we also used the BPRS and CGI scales (Timotijević & Paunović 2003). The age at onset of schizophrenia and the duration of psychosis were assessed using the medical history and the IRAOS (Häfner et al. 1992). For the current episode duration we used the part of IRAOS that marks episode development as 1=acute or sudden with duration within 7 days; 2=sub-acute within 1 week up to 1 month; 3=slowly, gradually developed episode more than a month, but cannot be dated exactly; and 9= unknown, cannot be evaluated.

Neurophysiologic examination was performed using EBNeuro Galileo Mizar 25. QEEG recordings which were performed between 9 a.m. – 1 p.m. while the subjects were awake with their eyes closed. During the recordings, vigilance was controlled by visual monitoring of the prominence of the alpha frequency in the posterior parts of the brain and regular verbal contacts were maintained with the subjects. The standard 10–20 electrodes placement system with 19 electrodes on the scalp and one on both earlobes were used in the recordings. The resistance was kept below 10 kΩ. The EEG digital recordings were screened visually and 25 x 2 second artifact-free epochs were selected from the background activity of the recording for subsequent analysis. As a result of the Fast Fourier Transformation, the averaged power spectral values of the delta (0.5–3.5 Hz), theta (4.0–7.5 Hz), alpha (8–12.5 Hz), and beta 1 (13–19.5 Hz) and beta 2 (20.0–29.5 Hz) bands were produced for each of the 19 scalp electrodes separately. Afterwards we analyzed the amplitude, the relative power and the mean frequency in the different bands. In order to obtain topography of the main region of interest the following electrode placements were chosen for further analysis: F3; F4; C3; C4; T3; T4; P3; P4; O1 and O2.

Statistical analysis

Statistical analyses of the data were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 13.0. The following non-parametric tests were used for demographic characteristics: Yates' chi-square, Fisher's exact and Mann Whitney test. Analyses of the clinical scale scores and QEEG parameters were performed with ANOVA and ANCOVA with covariate variables: age and duration of the disease.

RESULTS

The mean age of the patients was 34±9 for the male patients and 33.5±12 years for females (range: 18–55). Basic demographic and clinical characteristics are shown in table 1.

Table 1. Demographic and clinical characteristics of the schizophrenia patients

Item	Male	Female	Analysis (test)
Married	5 (50%)	8 (47.1%)	Yates's chi-square=0.06 df=1 p=0.8
Employed	10 (76.9%)	5 (29.4%)	Yates's chi-square=6.6 df=1 p=0.01
Handedness			
right-handed	6 (85.7%)	15 (100%)	Fisher's exact p=0.32
left-handed	1 (14.3%)	0	
Positive family history	3 (23.1%)	7 (41.2%)	Fisher's exact p=0.31
Hospital treatment	10 (76.9%)	14 (82.3%)	Fisher's exact p=1.0
Previous treatment	7 (53.8%)	15 (88.2%)	Fisher's exact p=0.049
Recidives	11 (84.6%)	14 (82.3%)	Fisher's exact p=1.0
Duration of current episode			
acute	3 (23.1%)	4 (23.5%)	Mann-Whitney test U=97.0 p=0.57
sub-acute	6 (46.1%)	5 (29.4%)	
chronic	4 (30.8%)	8 (47.1%)	

The subjects were not significantly different in their demographic characteristics (marital status, handedness, family history) except for employment (women had a worse occupational history than men). Regarding the course of the disease in the aspects of previous recidivism and treatment, hospital treatment, and the duration of the current episode, the only difference found was that female patients were treated more frequently compared to males.

The distribution according to the diagnosis of schizophrenia is presented in table 2. Although there was no statistical difference, male patients tended to be diagnosed with the paranoid and hebephrenic types of schizophrenia and female patients with the undifferentiated or unspecified types of schizophrenia.

Mean duration of illness (in months), age at onset in years and age of onset in patients with a positive family history are shown in table 3. In our study there were no statistical differences except for the disease duration which was longer in female patients.

Table 2. Distribution according to the diagnosis of schizophrenia

Schizophrenia	N	M/F ratio
paranoid	10	6/4
hebephrenic	6	4/2
catatonic	1	1/0
undifferentiated	6	2/4
residual	1	0/1
simple	2	0/2
unspecified	4	0/4

The results of the assessment of the symptoms of schizophrenia with clinical scales are presented in table 4. Female patients scored higher than males in the PANSS total score, the score of the PANSS positive subscale and in the BPRS score. Although not statistically significant male patients tended to present a higher score on the negative subscale of PANSS.

Table 3. Analysis of age of onset and duration of the disease

Item	mean±SD		ANOVA			ANCOVA
	male n=13(43.3%)	female n=17(56.7%)	F	df	p	p
Age (years)	34±9.1	33.5±12	0.018	1	0.89	0.62 ^a
Education (years)	11.5±1.2	11.8±2.5	0.09	1	0.77	0.8 ^b
Age at onset (years)	26.2±6.9	25±7.4	0.22	1	0.64	0.62 ^b
Age at onset (years, #)	24.3±1.5	24.6±7.7	0.003	1	0.96	0.11 ^b
Duration of illness (months)	91.8±89.1	116.5±86.1	8.7	1	0.059	0.048 ^c

^a duration of illness as a covariate; ^b age and duration of illness as covariate; ^c age as covariate; # patients with positive family history

Table 4. Statistics of the assessments with clinical scales

Clinical scale	mean±SD		ANOVA / MANOVA*	
	male n=13(43.3%)	female n=17(56.7%)	F	p
BPRS total score	32.6±8.8	37.9±10.3	F=3.94	<0.05
PANSS score	85.8±11.3	95.3±17.3	F=4.10	<0.05
PANSS negative subscale	10.4±6.5	7.4±4.2	F=1.37	>0.05
PANSS positive subscale	4.7±2.7	6.1±4.2	F=3.82	<0.05
CGI	5.0±1.3	5.2±0.9	F=0.34	>0.05

*age and duration of illness are independent variables

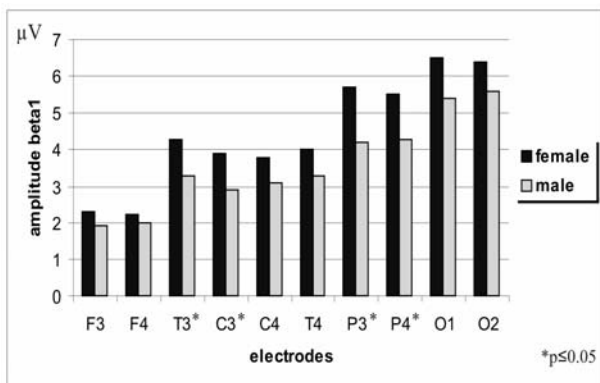


Figure 1. Distribution of gender differences in the beta 1 amplitude

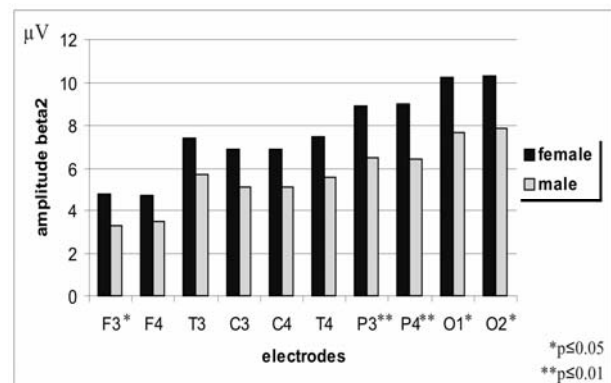


Figure 2. Distribution of gender differences in the amplitude in the beta 2 band

In the QEEG analysis for amplitude of the basic activity, there were no significant differences between male and female patients except for the beta 1 and beta 2 bands. Distribution of gender differences in the amplitude (μV) of the beta 1 and beta 2 bands are shown in figure 1 and 2 respectively. Female patients, compared to male, have more pronounced amplitude over the left central, temporal and parietal regions in the beta 1 activity, and the difference in amplitude for beta 2 activity is even more pronounced and present over the parietal and occipital regions bilaterally.

When we analyzed the mean frequency in the different bands of the basic activity the only statistical significance was found for the theta activity range, over the left frontal and temporal regions in female schizophrenic patients. Results are presented in figure 3.

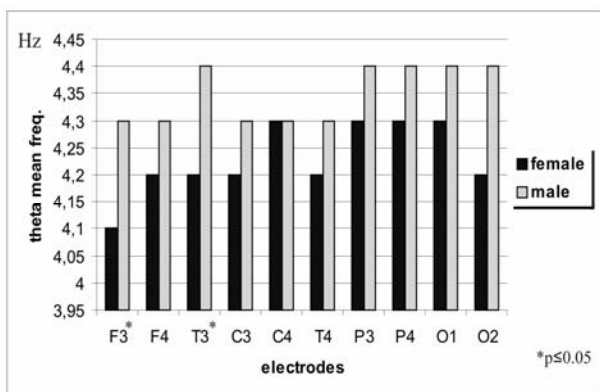


Figure 3. Distribution of gender differences in mean frequency in the theta band

Quantitative EEG analysis for the relative power of the different frequency bands showed gender differences in the beta 2 activity in female patients in the left frontal and in the occipital regions bilaterally. The results are presented in figure 4.

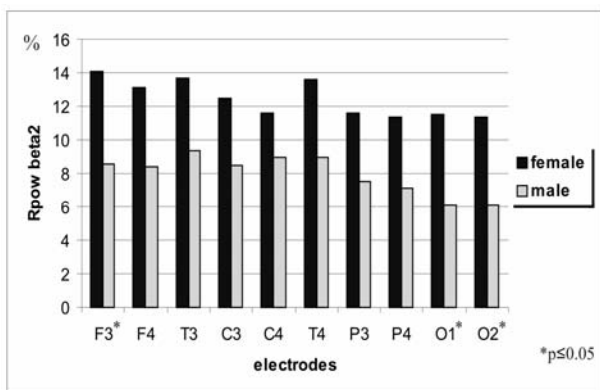


Figure 4. Distribution of gender differences in relative power of the beta 2 band

DISCUSSION

This study refers to the gender differences in some QEEG parameters such as amplitude, mean frequency and relative power of the different frequency bands in

the basic activity of schizophrenia patients. We also examined the gender differences in the duration of illness, age at onset, presented clinical psychopathology and some demographic characteristics. The main findings in our study were that female patients tend to have more pronounced beta activity: over central, temporal and parietal regions mainly on the left hemisphere for beta 1; and also, over parietal and occipital regions for beta 2 activity. Female patients also presented more severe positive symptomatology, had a longer disease duration and were more frequently treated with medication than males, and had a worse occupational history. Men were more often diagnosed with the paranoid and hebephrenic forms of schizophrenia and women with the undifferentiated or unspecified form according to ICD-10 criteria. By contrast, female patients were more likely to have more severe positive symptoms of the disease with higher scores in BPRS, PANSS scale and PANSS positive subscale when compared with male patients. This finding is consistent with the previous observation that female patients display more affective symptoms, auditory hallucinations and persecutory delusions with more rapid and greater responsiveness to antipsychotics (Taylor & Langdon 2006), but in this review, males have consistently an earlier onset and show more negative symptoms. Even though nonsignificant, we found greater scores on the PANSS negative subscale in the male patient group, which is similar to the other previous study (Moriarty et al. 2001).

Taking into consideration the previously discussed results we can conclude that our findings of increased amplitude and relative power in the beta band of the basic EEG activity in female patients represents the neurophysiologic aspects of the pronounced presence of positive symptoms of schizophrenia in female patients. This is in accordance with some recent studies (Slewa-Younan et al. 2004). A similar correlation between absolute powers in beta frequency band and clinical parameters measured with the PANSS scale was found in the beta range over the frontal-central areas on the left side, which were significantly correlated with the positive subscale and total PANSS score (Gross et al. 2006). Some previous studies positively linked BPRS scores and anxiety with the beta bands (Gattaz et al. 1992) and found an increase of beta activity over the left frontal and temporal regions (Saletu et al. 1990). Increase in beta 1 power was found in another study (Gschwandtner et al. 2009), but was positively correlated with negative symptoms of schizophrenia. We would like to point out consistently reported findings that beta activity is increased with anxiety/expectation (Lopes da Silva 1991) and with psychopathology in schizophrenia (Hughes & John 1999, Boutros et al. 2008). Psychotic symptoms are most likely a consequence of the dysfunction of multiple cortical areas and sub-cortical brain structures in patients with schizophrenia (Friston & Frith 1995) mainly in the left temporal and also in the right prefrontal areas which are

described as being specific for auditory hallucinations (Gaser et al. 2004, Nenadic et al. 2010). This could be a possible explanation of the lower mean frequency in the theta band in female patients who presented positive symptomatology (mainly hallucinations) in our study.

The gender differences at age of onset of schizophrenia are the most frequently reported with an earlier onset in male patients. In our study there were no gender differences in the age of onset, but when we account for the patients with a positive history, the age of onset of the disease was two years earlier in both gender groups which points to the genetic aspects of schizophrenia. Our finding is similar with other studies which did not find gender differences in the age of onset in different countries (Kendler & Walsh 1995, Aleman et al. 2003, Tang et al. 2007). Another gender difference in our study is that female patients were significantly less likely to be employed, which could be a result of some cultural aspects of the disease that are not in the scope of this investigation.

Our research suggested that female patients are more frequently treated than male which could be explained by their good relationship with the caregivers that appears to be stronger and longer lasting for females, as has been found in some other studies (Seeman 2004). A possible explanation for the previously noted difference in treatment received may be the data showing that in our study female patients had a longer duration of the disease (116,5 months) when compared to males (91,8 months). This is in opposition to the finding that men have more hospitalizations and longer in-patient stays than women (Usall et al. 2003, Taylor & Langdon 2006).

Our study has a number of limitations that need to be acknowledged. The sample has a small number of subjects with a heterogeneous group of schizophrenia types and with different lengths of illness. We have no control group. Also, the patients were drug-free only two days before the QEEG examination. In order to avoid the influence of the medications on the QEEG results in the future studies patients should be without any psycho-pharmacotherapy (including benzodiazepine) for a longer period of time.

CONCLUSION

Our study showed significant gender differences in the beta activity range in QEEG parameters, presented psychopathology, duration of illness, treatment received and unemployment in female patients. These QEEG findings could be explained by the severity of the presented psychopathology as measured with clinical rating scales. However, these findings need to be verified by future research with a larger sample size that includes either drug-naïve patients or patients that had not been taking any psychoactive drug one month before the study.

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