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QUANTITATIVE ELECTROENCEPHALOGRAPHY IN SCHIZOPHRENIA AND DEPRESSION

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SUMMARY

Background: *Standard (qualitative) electroencephalography (EEG) is routinely used in the diagnostic evaluation of psychiatric patients. Quantitative EEG (qEEG) findings differ between patients with schizophrenia, patients with depression, but results are not consistent. The aim of our study was to determine the differences in qEEG parameters between patients with schizophrenia, patients with depression, and healthy subjects.*

Subjects and methods: *The study included 30 patients with schizophrenia, 33 patients with depression, and 30 healthy subjects. All study participants underwent standard EEG. Artifact-free 100-second epochs were selected from the recorded material and analyzed with Fast Fourier Transformation (FFT) analysis.*

Results: *The results are presented as absolute spectral power values (μV^2) of delta, theta, alpha, and beta components of the EEG spectrum. EEGs were recorded from 12 locations including Fp1, Fp2, F3, F4, F7, F8, T3, T4, P3, P4, O1, and O2. In comparison with healthy subjects, patients with schizophrenia showed increased delta, theta, and beta activity and decreased alpha activity. Similar results were obtained in patients with depression, but in fewer regions. In patients with schizophrenia, delta power over Fp1, Fp2, F4, and F8 regions was increased in comparison with those in patients with depression. Interhemispheric asymmetry was found in patients with schizophrenia and healthy subjects, but not in patients with depression.*

Conclusion: *The finding that patients with schizophrenia differed from patients with depression in delta power values could be potentially used in differential diagnosis between schizophrenia and depression. The role of qEEG in clinical differentiation between these two mental disorders may be especially important in cases of negative-symptom schizophrenia.*

Key words: *quantitative electroencephalography - schizophrenia - depressive disorder*

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INTRODUCTION

Among the biological indicators of mental diseases, electrophysiological findings hold an especially important place. Quantitative electroencephalography (qEEG), along with the evoked potential technique, is the most frequently used method in electrophysiologic studies. Previous research has shown that psychiatric patients exhibit various qEEG abnormalities, which are present in up to 80% of psychiatric patients as opposed to only 10% of healthy subjects (Coburn et al. 2006).

There are practically no qEEG studies in mental disorders that did not find some qEEG abnormalities (John 1989). However, the integration of the qEEG in psychiatric practice has been a slow process (Coutin-Churchman et al. 2003) and the method is still not used in the routine diagnostic evaluation of psychiatric patients (Nuwer 1998). The main reason for the currently limited clinical use of qEEG are inconsistent, or even contradictory, results obtained by qEEG studies in mental disorders (primarily schizophrenia) (John et al. 1994). Due to this inconsistency in research results, studies need to be repeated and combined with other research and diagnostic methods (neuroradiological, biochemical, neuropsychiatric, genetic).

Previous qEEG studies mostly investigated schizophrenia and depression. In patients with schizophrenia, abnormal changes in the EEG pattern can be found in 5-80% of the cases (Shagass 1977). Furthermore, qEEG findings in schizophrenia show a wide range of abnormalities. The most frequently reported qEEG abnormalities include increased slow activity (Miyauchi et al. 1990, Boutros et al. 2008, Knyazeva et al. 2008) and decreased alpha activity (Gambini et al. 1990, Sponheim et al. 1994) which is normalized after antipsychotic medical treatment (Moore et al. 1997, Begić et al. 2000a). Such changes can be noticed over all regions, but mostly over the frontal regions. The most frequent finding in schizophrenia is an abnormal frontal asymmetry of alpha power (Jetha et al. 2009). Differences in qEEG can even be found between different subtypes of schizophrenia ("positive-symptom" vs. "negative-symptom" schizophrenia) (Gerez & Tello 1995, Begić et al. 2000b). There are also differences in qEEG indicators between patients with particular clusters of schizophrenic symptoms (Gross et al. 2006). According to the conventional EEG studies, 20-40% of patients with depression have abnormal EEG findings (Galderisi et al. 1997, Hughes & John 1999). Quantitative EEG studies in patients with depression found increased slow wave activity (Adler et al. 1999), decreased slow wave acitivity (Davidson 1992) and increased alpha and beta activity (Pollock & Schneider 1990). Differences in qEEG indicators were found even

between unipolar and bipolar depressive disorders (Prichep & John 1992). Asymmetry in EEG activity over frontal regions in depression was also reported (Debener et al. 2000, Knott et al. 2001, Allen et al. 2004, Vuga et al. 2006). The most consistent findings in depression were abnormal qEEG indicators (decreases in prefrontal cordance; left-right asymmetry of combined theta + alpha power) predictive of therapeutic response (Leuchter et al. 2002, Bares et al. 2007, Iosifescu 2008).

Many studies compared patients with schizophrenia or depression with healthy subjects, whereas only a few studies compared schizophrenia and depression. One of such studies (Fink et al. 1965), based on the spectral analysis of EEG activity, found the differences between these two mental disorders. More recent studies have confirmed that schizophrenia and depression differ in their qEEG indicators (Li & Fan 2005, Li et al. 2008).

Due to the scarcity of studies comparing schizophrenia and depression and possible role of qEEG in differential diagnosis between these two disorders, we performed the present study. The aim of the study was to compare qEEG findings in patients with schizophrenia, patients with depression, and healthy subjects. We wanted to determine if there were any differences in qEEG indicators between patients with schizophrenia and those with depression. The hypothesis was that schizophrenia and depression differ in qEEG indicators. Furthermore, we suppose that qEEG changes will be most pronounced in schizophrenic patients (in comparison with depressive and healthy examinees). Also, differences in the comparison of depressive and healthy ones are expected as well.

Specific qEEG findings in patients with schizophrenia and patients with depression may contribute to their clinical differentiation. Thus, the significance of qEEG parameters as possible biological markers of depression or schizophrenia would be confirmed.

SUBJECTS AND METHODS

Participants

The study was performed at the Department of Psychiatric, University Hospital Center Zagreb, in 2008 and 2009. It included 30 patients with schizophrenia (8 men), 33 patients with depression (7 men), and 30 healthy subjects (13 men). All patients were hospitalized and diagnosed with schizophrenia or depression according to the criteria of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV 1994) by two independent psychiatrists. Patients were either drug-naïve or had not been taking psychoactive drugs for one month before the study.

Healthy subjects with no previous history of psychiatric disorders were recruited from undergraduate and postgraduate students of the University of Zagreb School of Medicine and Faculty of Humanities and Social Sciences.

Participants who had neurological disease, head trauma, "soft" neurological signs, or history of EEG changes were excluded. All study participants were right-handed and all provided informed consent before inclusion in the study.

Methods

All study participants underwent conventional EEG registration. EEG recordings were performed with Nicolet's BEAM device in the morning hours, after the subjects had breakfast. During the EEG recording, subjects were in supine position, with their eyes closed. Electrodes were placed according to the international "10-20" system using linked-ears as a reference. Signals were digitized at 256 samples channel second with a low-frequency filter of 0.5 and a high-frequency filter of 30 Hz, and impedance levels were $\leq$5 kΩ. All EEG recordings were performed by the same EEG technician.

Epochs contaminated by blinks, eye movements, and movement-related artifacts were excluded from analyses by direct visual inspection of the raw data. Artifact-free 100 seconds period (five 20-second epochs) were selected from the recorded material and analyzed using Fast Fourier Transformation (FFT). The results were presented as absolute spectral power values (μV^2) for individual segments of EEG spectrum (delta (0.5-4.0), theta (4.0-8.0), alpha (8.0-13.0), and beta (13.0-30.0)). The observed regions included Fp1, Fp2, F3, F4, F7, F8, T3, T4, P3, P4, O1, and O2.

Statistical analysis

The Mann-Whitney non-parametric test was used to evaluate the differences between the groups, whereas the Kruskall-Wallis test was used to compare the symmetry of EEG activity between the left and right hemispheres. The level of significance was set at $p<0.05$. Data were analyzed with Statistical Package for the Social Sciences (SPSS), ver. 11.5. (SPSS Inc., Chicago, IL, USA).

RESULTS

We compared qEEG findings between patients with schizophrenia, patients with depression, and healthy subjects. The mean age (± standard deviation) in patients with schizophrenia, those with depression, and healthy subjects was 31.3±10.6, 55.1±12.6, and 35.9±10.1 years, respectively. Patients with depression were significantly older than the other two groups of participants ($F_{2.83}$=41.2; $p<0.001$). There was no significant correlation between age and qEEG parameters (the correlation ranged from -0.035 to 0.11). The average duration of schizophrenia was 4.8±3.0 years and of depression 5.2±3.3 years.

Median values and range of delta, theta, alpha, and beta rhythms in patients with schizophrenia, patients with depression, and healthy subjects are shown in Table 1.

Table 1. Median values (range) of eeg rhythms in patients with schizophrenia, patients with depression, and healthy subjects

Rhytm		δ			Θ	
Lead	Sch	Depr	Healthy	Sch	Depr	Healthy
Fp1	40.12 (180.8)	23.61 (238.1)	15.14 (46.8)	20.27 (245.5)	19.08 (311.7)	13.84 (44.1)
Fp2	49.08 (324.7)	22.93 (398.4)	14.54 (104.9)	18.22 (179.3)	17.46 (205.5)	16.51 (83.8)
F3	38.08 (138.9)	25.63 (238.0)	13.97 (56.3)	19.20 (554.2)	18.71 (314.6)	14.34 (43.1)
F4	42.50 (409.4)	18.44 (431.1)	13.81 (58.2)	24.05 (140.1)	20.51 (220.3)	15.78 (140.6)
F7	30.01 (161.7)	19.11 (280.3)	14.84 (51.1)	19.77 (456.9)	20.41 (250.6)	12.98 (56.9)
F8	38.25 (421.8)	19.51 (457.3)	15.8 (104.5)	24.13 (128.6)	18.97 (210.4)	16.12 (167.5)
T3	17.73 (79.6)	17.30 (241.8)	15.21 (47.7)	12.68 (461.8)	13.06 (255.4)	9.29 (51.32)
T4	22.71 (312.9)	14.09 (412.8)	15.24 (41.1)	12.68 (95.3)	14.56 (182.4)	10.63 (82.7)
P3	27.24 (170.3)	21.58 (232.6)	17.71 (43.5)	23.90 (447.9)	16.12 (254.9)	24.49 (101.6)
P4	34.16 (406.8)	20.35 (433.2)	9.2 (36.6)	28.09 (108.2)	22.49 (240.3)	13.63 (168.4)
O1	27.35 (110.7)	20.26 (271.8)	13.9 (82.7)	22.47 (721.8)	19.88 (228.9)	18.97 (95.05)
O2	36.39 (320.7)	18.98 (447.15)	8.66 (31.4)	19.60 (98.08)	22.80 (189.2)	12.54 (73.8)
Rhytm		α			B	
Lead	Sch	Depr	Healthy	Sch	Depr	Healthy
Fp1	27.13 (266.9)	25.32 (120.9)	61.75 (227.2)	27.63 (130.6)	38.40 (171.2)	18.29 (132.3)
Fp2	27.09 (127.3)	24.74 (240.9)	43.57 (277.8)	25.19 (112.7)	30.04 (140.6)	15.31 (76.1)
F3	29.30 (245.6)	30.37 (150.9)	70.45 (251.4)	30.97 (140.1)	36.22 (180.5)	21.92 (132.5)
F4	25.39 (137.85)	31.45 (230.7)	45.31 (303.1)	27.83 (140.3)	34.81 (156.7)	18.01 (70.9)
F7	19.44 (267.2)	21.12 (140.3)	41.09 (166.3)	26.15 (140.8)	45.29 (117.6)	19.91 (347.2)
F8	20.57 (92.39)	22.47 (283.8)	45.12 (251.7)	27.80 (156.3)	34.66 (141.8)	25.41 (112.4)
T3	13.82 (266.1)	18.08 (180.9)	25.66 (147.2)	18.12 (109.4)	26.81 (95.5)	20.62 (65.6)
T4	17.03 (75.3)	20.47 (221.5)	29.94 (201.9)	22.10 (167.4)	22.60 (169.8)	23.47 (57.9)
P3	47.45 (403.8)	52.48 (435.7)	92.93 (465.8)	37.04 (68.3)	34.38 (120.9)	42.03 (118.4)
P4	46.72 (303.1)	63.60 (503.8)	47.08 (292.1)	34.14 (129.7)	34.32 (139.7)	26.45 (115.4)
O1	45.060 (479.37)	60.19 (456.8)	56.92 (753.9)	33.08 (80.5)	41.23 (85.0)	23.25 (48.1)
O2	40.15 (290.7)	48.41 (350.6)	38.6 (630.9)	30.19 (148.6)	26.35 (80.1)	19.53 (55.1)

Sch - patients with schizophrenia; Depr - patients with depression; Healthy - healthy subjects

Table 2. Statistically significant differences of eeg rhythms between the groups (patients with schizophrenia, patients with depression, and healthy subjects)

Rhytm		δ			Θ	
Lead	Sch-Heal	Sch-Depr	Depr-Heal	Sch-Heal	Sch-Depr	Depr-Heal
Fp1	**	*	*			
Fp2	**	*	*			
F3	**		*			
F4	**	*		*		
F7	**			*		*
F8	**	*		*		
T3						
T4	*					
P3	*					
P4	**		**	*		
O1	**					
O2	**		**	*		
Rhytm		α			B	
Lead	Sch-Heal	Sch-Depr	Depr-Heal	Sch-Heal	Sch-Depr	Depr-Heal
Fp1	**		**	**		**
Fp2	*			**		**
F3	*		*	**		**
F4	*			**		**
F7	**		*			**
F8						*
T3	**					
T4	*					
P3						
P4						
O1						
O2				**		

** p<0,01; * p<0.05; Sch - patients with schizophrenia; Depr - patients with depression; Healthy - healthy subjects

Statistically significant differences between the groups are presented in Table 2.

The comparison between patients with schizophrenia and healthy subjects showed changes in all EEG activities. Power of delta activity in patients with schizophrenia was increased in comparison with that in healthy subjects over Fp1, Fp2, F3, F4, F7, F8, T4, P3, P4, O1, and O2 regions. Patients with schizophrenia had significantly higher theta power over F4, F7, F8, P4 and O2 regions than healthy subjects. Power of alpha activity was decreased over Fp1, Fp2, F3, F4, F7, T3, and T4 regions in patients with schizophrenia, whereas power of beta activity was increased over Fp1, Fp2, F3, F4 and O2 regions.

Comparison between qEEG findings in patients with depression and those in healthy subjects also showed differences in all segments of the EEG spectrum. Patients with depression had increased delta power values over Fp1, Fp2, F3, P4, and O2 regions and increased theta power over F7 region. In comparison with healthy subjects, patients with depression had decreased alpha power values over Fp1, F3, and F7 regions and increased beta power values over Fp1, Fp2, F3, F4, F7, and F8 regions.

The comparison of qEEG parameters between patients with schizophrenia and those with depression revealed fewer differences than reported previously (Popović-Knapić & Begić 2009, Begić et al. 2009). Patients with schizophrenia were found to have increased delta power over Fp1, Fp2, F4, and F8 regions in comparison with patients with depression.

We compared the values of individual segments of EEG spectrum with respect to presence (or absence) of interhemispheric asymmetry for each of the groups. Asymmetry was found in patients with schizophrenia and healthy subjects, but not in patients with depression.

Patients with schizophrenia had increased delta power in the right frontal region (Fp2 - Fp1) and increased theta power in the right temporal region (T4 - T3). Healthy subjects had increased delta and alpha power values in the left parieto-occipital regions (P3 - P4, O1 - O2). In patients with depression, asymmetry was not found either in EEG activity or any of the regions.

DISCUSSION

Schizophrenia

The symptoms of schizophrenia are caused by the dysfunction of multiple cortical and subcortical brain structures (Gross et al. 2006), which may explain inconsistent and sometimes contradictory qEEG findings in these patients. In the present study, qEEG changes in schizophrenic patients in comparison with healthy subjects were found in all segments of the EEG spectrum. With respect to the topographic distribution, most EEG abnormalities were found over occipital regions, followed by central and occipital regions. Abnormalities in qEEG over so many regions in patients with schizophrenia could be associated with disturbed neural circuits in schizophrenia (Benes 2000).

Changed power values of all EEG activities over frontal regions in patients with schizophrenia are compatible with "hypofrontality". Hypofrontalitiy is lower metabolic activity in the frontal regions of the brain during an attention task, as a possible early marker of schizophrenia. Many brain imaging studies using different methods also reported on "hypofrontality" in schizophrenia (Winterer et al. 2000, Hazlett et al. 2000). Positron emission tomography studies in patients with this mental disorder found decreased metabolism in frontal brain regions (Winterer et al. 2000) and increased metabolism in the basal ganglia (Volkow et al. 1986). The changes in the basal ganglia volume are observed in schizophrenic patients (Mamah et al. 2007), although there are investigations which have not found differences in the size of these areas (Gunduz et al. 2002). The reduction in the anterior amygdale-hippocampal complex in schizophrenia has been also registered (Anderson et al. 2002). Thus, it is believed that neocortical-striatal-thalamocortical dysfunction is associated with dopaminergic dysbalance (Carlsson 1995). In addition to frontal dysfunction, fronto-limbic dysfunction was also observed in patients with schizophrenia (Bilder et al. 2000). This observation could explain numerous qEEG changes over frontal regions found in these patients in the present study.

EEG asymmetry over frontal (delta power) and temporal (theta power) regions could be associated with the reduction in the gray matter of the limbic areas (Gross & Huber 2008) or in the gray matter of the superior temporal gyrus (STG) (Anderson et al. 2002), cortical atrophy (Mientus et al. 2002).

and increased volume of brain ventricles (Ardekani et al. 2005). Changes in theta and alpha activity may indicate GABA-ergic inhibition of the thalamus (John et al. 2007). This primarily refers to the alpha activity generated in the thalamus. From the electrophysiological point of view, hallucinations in schizophrenia are associated with increased theta activity in the STG (Ishii et al. 2000). Increased beta activity in patients with schizophrenia included in our study was consistent with that reported previously (Dierks 1992, Saletu et al. 1990). One of the reasons of increased beta activity in patients with schizophrenia could be damage to the deeper brain structures (Dierks 1992).

Depression

There are many areas of the brain responsible for emotions and mood. The neuronal circuit responsible for emotions consists of dorsolateral and ventromedial prefrontal cortex, n. accumbens, basal ganglia, amygdales, temporal and parietal cortex, and hypocampus (Deslandes et al. 2008). Lesions to these structures in patients with depression elicit EEG changes. In our study, comparison between patients with depression and healthy subjects showed that patients with depression had significantly higher delta and theta power values. Increased alpha and beta activity was also found in patients with depression in comparison with healthy subjects. Changes in alpha rhythm are associated with thalamic dysfunction, but they are also associated with cortical activity. It is known that alpha power is reversely proportional with cortical activity in patients with depression (Pollock & Schneider 1990).

Many studies found qEEG asymmetry in patients with depression (reduced activity over the left frontal region). According to the metabolic and neuroimaging studies, this asymmetry is associated with dysfunction of the left hemisphere (prefrontal cortex and basal ganglia) (Fregni et al. 2006). Our results did not confirm asymmetry in EEG activity in patients with depression. There are several possible explanations for this finding. First, it is known that antidepressants (and benzodiazepines) decrease or remove this asymmetry in patients with depression (Henriques & Davidson 1991, Davidson et al. 1992). It is possible that the drug-free period in our study was too short. Second, it is not clear to what extent EEG parameters are influenced by general health status and physical activity (Morgan et al. 2005). Such influence was not controlled for in our study. Third, some of our patients with depression had been undergoing outpatient psychotherapy treatment before entering the study. We cannot say if psychotherapy could influence biological parameters of cortical activity (and, consequently, qEEG) and in what manner.

Schizophrenia vs. depression

The group of schizophrenic and depressive patients differed in age, what could not be avoided, because we wanted to compare those entities after lasting for many years. As schizophrenia most often occurs between the 15^{th} and 25^{th} year of age, and depression at the turn from the thirties into forties, these two groups differ regarding age, but not in the duration of illness. Therefore, the average duration of illness did not differ in these two groups. The effect of age upon EEG in depressive examinees will be discussed later.

Comparison between patients with schizophrenia and those with depression showed increased delta power values over Fp1, Fp2, F4, and F8 regions in patients

with schizophrenia, which is in accordance with some previous findings (Hazlett et al. 2000, Sponheim et al. 2000). These results confirm that schizophrenia and depression have different biological basis, despite the fact that both disorders differ from healthy subjects in a wide range of similar or identical findings. Nevertheless, the question remains whether it is possible to discern between these two disorders, especially between negative-symptom schizophrenia and depression, on the basis of qEEG parameters.

There are several limitations to our study, which could bias the results. The sample size of each group was relatively small, which could influence the stability of the data, especially in the view of large variations in qEEG parameters. Furthermore, there were significant differences in age between participants with depression and other two groups. Although our results showed zero-correlation between age and qEEG parameters, future studies should control for this parameter. Some previous investigations suggest that prefrontal cordance in depressed patients is not significantly affected by factor of age (Morgan et al. 2005).

CONCLUSION

Future studies should also use a larger sample size and longer drug-free period before the study as well as control for more factors (psychotherapy, general health status, physical activity, and prognostic outcome) in order to provide more accurate answers about the use of qEEG in differential diagnosis between schizophrenia and depression.

Quantitative EEG cannot provide answers about etiologic basis of these disorders, because brain rhythms recorded from the surface of the scalp may reflect many different pathoanatomical changes. However, given that it is a routine diagnostic method, the knowledge that different disorders have different EEG manifestations may have utility in distinguishing between schizophrenia and depression.

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