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EEG correlates of a mental arithmetic task in patients with first episode schizophrenia and schizoaffective disorder

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HIGHLIGHTS

- EEG characteristics of patients with schizoaffective disorder at rest are instantiated by increased theta and beta powers and decreased alpha powers, which are less pronounced but similar to schizophrenia.
- In schizophrenia patients the spectral power of slow and fast frequency bands decreases during the performance of a mental arithmetic task.
- During task performance schizoaffective patients demonstrate a decrease of slow frequency bands as in schizophrenia and an upward trend of gamma power increase alike healthy individuals.

ABSTRACT

Objective: To evaluate the spectral power of the cortical bands in patients with first episode schizophrenia and schizoaffective disorder at rest and during the performance of a mental arithmetic task.
Methods: We analyzed EEG spectral power (SP) in the resting state and subsequently while counting down from 200 in steps of 7, in 32 first episode schizophrenia patients (SZ), 32 patients with first episode schizoaffective disorder (SA) and healthy controls (HC, $n = 40$). Behavioral parameters such as accuracy and counting speed were also evaluated.
Results: Both SZ and SA patients were slower in counting than HC, no difference was obtained in the accuracy and counting speed in the patient groups. In the resting state patients showed elevated midline *theta* power, off-midline anterior *beta 2* power and decreased central/posterior *alpha* power. The SA group occupied an intermediate position between the schizophrenia patients and controls.
In task performance patients lacked a typical increase of midline *theta*, left anterior *beta 2*, and anterior *gamma* power; however, schizoaffective patients demonstrated a growing trend of power in the *gamma* band in left anterior off-midline sites similar to HC. Moreover, *alpha* power was less inhibited in schizoaffective patients and more pronounced in schizophrenia patients indicating distinct inhibitory mechanisms in these psychotic disorders.
Conclusions: Patients with SA demonstrate less alteration in the spectral power of bands at rest than SZ, and present spectral power changes during cognitive task performance close to the controls.
Significance: Our study contributes to the present evidence on the neurophysiological distinction between schizophrenia and schizoaffective disorder.

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1. Introduction

Whether schizoaffective disorder is a distinct clinical entity, a variant of schizophrenia or an affective disorder is a matter of continual debate (Evans et al., 2009; Abrams et al., 2008; Peralta and Cuesta, 2008; Cotton et al., 2013; Wilson et al., 2014). The proximity of the initial presentation of psychotic symptoms in first episode schizophrenia (SZ) and schizoaffective disorder (SA) often results in these groups being merged together into one experimental sample. However, from a neuropsychological and neurophysiological perspective, along with the similarities with schizophrenia, schizoaffective patients exert various specific psychophysiological and cognitive characteristics (Abrams et al., 2008; Zaytseva et al., 2011). Thus, a MEG study exploring the localization of magnetic sources for auditory M100 signals reported different source localization in the auditory cortex in schizophrenia and schizoaffective disorder (Teale et al., 2000). In a more recent study, Mathalon et al. (2010) using event-related potentials showed normal P300 amplitudes for the auditory and visual stimuli, although the latency and reaction time were close to schizophrenia.

Cognitive research conducted over the last decade suggests that schizoaffective disorder has an intermediate phenotype between schizophrenia and affective disorders (Gooding and Tallent, 2002; Stip et al., 2005). However, it has been reported that the general contour of cognitive impairment in patients with schizoaffective disorder is close to schizophrenia (Evans et al., 2009).

There is a growing body of evidence suggesting that cognitive dysfunction is associated with the abnormal synchronization of oscillatory activity in low and high band frequencies (Ford and Mathalon, 2008; Ford et al., 2012; Uhlhaas and Singer, 2010). Alterations of neuronal oscillations in schizophrenia have been demonstrated in a resting state in schizophrenia: meta-analysis of Boutros et al. (2008) revealed the preponderance of slow rhythms in schizophrenia patients and a reduction in high-frequency activity (Rutter et al., 2009). The most significant difference in schizophrenia patients compared to healthy subjects, depressive and schizotypal patients has been found in theta and delta activity, which is increased in the frontal-temporal regions of the brain (Guich et al., 1989; Pascual-Marqui et al., 1999; Sponheim et al., 2000). The predominance of slow-wave activity in the frontal regions with reduced blood flow and slowing glucose utilization in frontal areas, especially during the cognitive load, is considered to be the "electrophysiological equivalent" of hypofrontality (Ingvar et al., 1976; Guich et al., 1989; Williamson et al., 1989).

Several studies have investigated the relation between the resting EEG parameters in various schizophrenia subtypes. It has been shown that patients with an early onset of schizophrenia exhibited increased spectral power of slow rhythms, thus, the alpha rhythm was mostly decreased (Fenton et al., 1990; Sponheim et al., 2000; Mientus et al., 2002). However, only one study demonstrated spectral power differences in the resting condition in schizophrenia and schizoaffective disorder. It demonstrated a substantial increase in delta-1 and theta-1 spectral powers, which was suggested as being a "schizophrenic EEG component" and a shift in the peak frequency at rest to the slower alpha-1 range – "an affective EEG component" (Schellenberg et al., 1990).

The aim of our study was to evaluate task induced brain activity by means of EEG spectral power in clinically homogenous groups of patients with first episode schizophrenia and schizoaffective disorder. We hypothesize that processing of a cognitive task may underline distinct neuronal activity in schizophrenia and schizoaffective groups. Besides, the inclusion of patients with the first episode of psychosis allowed us to study EEG correlates regardless of the confounding effect of duration of the illness with a minimal effect of medication. We assumed that the analysis of EEG spectra and behavioral parameters during a cognitive task would reveal certain biological patterns that are specifically related to schizophrenia or schizoaffective disorder.

2. Methods

2.1. Participants

In total, 64 patients with first episode psychosis in the acute/sub-acute phase were enrolled into the study. Patients were recruited on admission to the Early Intervention Clinic at the Moscow Research Institute of Psychiatry. All of the patients underwent clinical assessment and a structural diagnostic interview during the first week after admission by three experienced physicians with specialty training in schizophrenia. Diagnosis was based on ICD-10 and was confirmed in a 1-year follow-up. Patients were assigned into 2 groups according to the diagnosis: 32 patients with schizophrenia (**SZ**, F.20.0, F.20.2, F.20.3, F.20.6) and 32 patients with schizoaffective disorder with depressed and bipolar subtypes (**SA**, F.25) (World Health Organization, 1992). All of the groups had an equal number of males and females. There were no differences between the three groups with respect to age ($F = 0.28$, df = 101, $p = 0.75$) and years of education ($F = 0.83$, df = 101, $p = 0.48$). Symptoms were rated using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) during the first week of hospitalization on the day of EEG recording. Inter-rater reliability was no more than one point above or below the initial rate of each item. The SZ patients had more severe positive ($t = 3.14$, df = 62, $p = 0.002$) and negative ($t = 2.74$, df = 62, $p = 0.007$) symptoms according to their PANSS scores than patients with SA.

All of the patients were on antipsychotic therapy with an average duration of 1 week. Ten patients (6 schizophrenia patients and 4 patients with schizoaffective disorder) were drug naive. Twenty-six patients were receiving monotherapy with atypical antipsychotics, while the remaining 28 patients with schizoaffective disorder received combination treatments of antidepressants or anticonvulsants and atypical neuroleptics. None of the patients received typical neuroleptics and none of the patients was treated with anticholinergic drugs or benzodiazepines. The patient groups did not significantly differ in their average chlorpromazine equivalent (CPZ) daily dosage ($t = 0.92$, df = 52, $p = 0.36$).

A control group of 40 healthy volunteers was recruited from the research database of the Moscow Research Institute of Psychiatry (**HC**). All of the participants were right-handed. The overall exclusion criteria were: brain injury, comorbid neurological disorders, somatic illnesses compromising the central nervous system, or an active diagnosis of substance abuse. The demographic and clinical characteristics of all of the groups are shown in Table 1.

The study was approved by the local Ethic Committee and all of the participants signed the informed consent.

2.2. Tasks and behavioral data

Participants underwent an EEG procedure which was performed in the resting state (with eyes closed) and during the cognitive task-mental arithmetic (with eyes closed). We used standard Kraepelinian counting with the instruction to count down from 200 in steps of 7 within a time limit of 100 s. All of the subjects had to provide their feedback at the end of the task on the result of the counting. For each subject we calculated the parameters of accuracy (1 – correct, 0 – not correct) and the speed of counting (number of counting steps/100 s.). Accuracy data were available for 70 participants (26 – controls, 26 – schizophrenia patients, 24 – schizoaffective disorder patients). The subsets of the groups with the task accuracy

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Table 1
Demographic and clinical characteristics of the groups.

Variable and *P*-value	Schizophrenia (SZ) *n* = 32				Schizoaffective disorder (SA) *n* = 32				Healthy control (HC) subjects *n* = 40			
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max
Age (years) HC = SZ; HC = SA; SZ = SA	28.91	10.64	19	54	27.59	6.93	18	46	27.63	6.37	19	47
Education (years) HC = SZ; HC = SA; SZ = SA	13.47	1.50	10	15	13.75	1.87	10	15	14.05	2.19	9	18
Handedness	32 right				32 right				32 right			
Gender	16 female, 16 male				16 female, 16 male				20 female, 20 male			
PANSS positive SZ > SA*	19.34	5.58	7	34	15.34	4.55	8	25				
PANSS negative SZ > SA**	17.09	4.62	10	27	13.97	4.48	7	25				
PANSS general SZ > SA*	41.50	7.55	30	56	37.41	6.71	27	53				
Diagnosis subtype	Paranoid schizophrenia (*n* = 32)				Schizoaffective disorder, manic type (*n* = 5) Schizoaffective disorder, depressive type (*n* = 27)							
Age at illness onset SZ = SA	28.78	10.54	18	54	26.65	6.77	19	41				
Chlorpromazine equivalent SZ = SA	Mean = 227.55/ SD = 69.10				Mean = 208.62/SD = 80.90							

* $p < 0.05$ with t test independent by group.
** $p < 0.01$ with t test independent by group.

data didn't differ from the main sample in terms of age (for HC– $F = 0.90$, df = 64, $p = 0.35$; SZ – $F = 0.01$, df = 56, $p = 0.92$; SA – $F = 0.24$, df = 54, $p = 0.63$); gender (HC – $\chi^2 = 0.09$, df = 64, $p = 0.76$; SZ – $\chi^2 = 0.33$, df = 56, $p = 0.57$; SA – $\chi^2 = 0.37$, df = 54, $p = 0.54$); and years of education (HC – $F = 0.73$, df = 64, $p = 0.40$; SZ – $F = 0.09$, df = 56, $p = 0.76$; SA – $F = 0.26$, df = 54, $p = 0.61$).

2.3. EEG acquisition and data preprocessing

Biopotentials were recorded from 19 electrodes: Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, O1, O2 and midline sites (Fz, Cz, Pz) according to the "International 10-20 System" (Jasper, 1958). Reference electrodes were placed on the linked earlobes. High frequency filters were set at 70 Hz, at a time constant of 0.3 s. EEG traces of 100 s were recorded and quantified at 200 Hz by an EEG mapper from the company MBN, Russia. All electrode impedances were maintained at or below 10 kOhm, with most EEG sites near 5 kOhm.

EEG editing included a custom designed multiple-source eye correction method (Novototskii-Vlasov et al., 2007) with subsequent rejection of the EEG segments that contained eye movement contaminations and muscle artifacts. From the 100s EEG-record 10–15 five-second artifact-free intervals were chosen by an expert. These EEG segments underwent fast Fourier transform (FFT) with subsequent averaging and obtaining of the individual averaged power spectra for each frequency band.

2.4. Data analysis

Spectral power (SP) of 6 frequency ranges: delta (1.5–3.9 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta1 (13–19 Hz), beta2 (20–29 Hz), gamma (30–40 Hz) was calculated and compared in three groups. Mean power (μV^2/Hz) was computed across epochs. Prior to the statistical analysis, the spectral powers were logarithmically transformed in order to obtain a normalized distribution.

2.5. Statistical analysis

Statistical analysis was performed using STATISTICA 6.0 software. Demographical parameters and clinical correlates (PANSS scores) were compared between the groups using a t-test. Non-parametric statistics were used to analyze the between-group differences in counting accuracy and speed due to Non-Gaussian distribution.

Statistical analyses of SP (natural logarithm of spectral power) were performed using 3-Factorial Analyses of Variance (ANOVAs) including "GROUP" (SZ, SA, HC), "CONDITION" (Rest vs. Task), "REGION OF INTEREST" (ROI) factors. Electrodes within the defined ROIs were unified. We used the values of the SP for each selected electrode within the defined ROI by applying the multivariate test criteria (Vasey and Thayer, 1987). Thus, the anterior ROIs included Fp1, F3, F7 (ROI1) and Fp2, F4, F8 (ROI2); the central and posterior ROIs included C3, P3, O1, T3, T5 (ROI3) and C4, P4, O2, T4, T6 (ROI4). The data was analyzed separately for the anterior, central/posterior sites and midline sites. The statistical analysis for SP in midline sites comprised the "Electrode" factor (Fz, Cz, Pz) in order to elicit more localized group differences.

Subsequently, between-group and within-group comparisons of spectral power in the resting state and during task performance were done using repeated-measures ANOVA for each frequency band with electrodes as repeated measures; the differences were estimated with least squares post hoc tests (Fisher LSD). Greenhouse–Geisser corrections were applied to correct for violations of sphericity and homogeneity. To take into the account the fact that multivariate analysis was conducted for 6 frequency bands, a Bonferroni corrected value of $p = 0.008$ was regarded as significant.

Correlations between EEG spectral power values in the resting state and the in-task condition as well as related behavioral measures and PANSS scores were obtained for each diagnostic group using Spearman correlation coefficients.

3. Results

3.1. Behavioural task performance measures

The number of correct answers (accuracy) in counting was similar in all 3 groups (HC, SZ and SA ($\chi^2 = 0.387$, df = 2, $p = 0.82$). The counting speed (number of steps) 0.285 ± 0.11 s/s in controls,

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0.196 ± 0.09 s/s in SZ and 0.199 ± 0.08 s/s in SA was significantly higher in controls than in SZ ($Z = 2.731$, $p = 0.006$) and SA ($Z = 2.807$, $p = 0.005$). There was no difference in counting speed between the patient groups ($Z = -0.243$, $p = 0.808$).

3.2. Comparisons of EEG spectral power in the resting and in-task conditions.

3.2.1. Between-group comparisons

As we focused on the effects of "Group" and "Condition", we analysed their effects in the interaction with the other factors. ANOVA results for midline, off-midline anterior and central/posterior areas are summarized in Tables 2–4, respectively. We found the main effect of "Condition" in the *theta* frequency band in the midline sites; in anterior frontal regions there was a significant main effect in the *beta 2* band. In central/posterior sites, the main effect was found in the *alpha* band.

In the resting condition midline *theta* power in Fz was higher in SZ than in HC ($p < 0.001$) and in SA ($p < 0.05$), [ELECTRODE × GROUP, $F(4,174) = 5.32$, $p < 0.001$]. *Theta* power in Pz was higher in the SA than in the SZ group ($p < 0.05$).

The SZ patients also had lower *alpha* power in the off-midline central, parietal and occipital sites than the HC ($p < 0.05$) and SA patients ($p < 0.05$) [ELECTRODE × ROI × GROUP, $F(8,404) = 2.65$, $p = 0.019$; for left ROI: ELECTRODE × GROUP, $F(8,404) = 6.37$, $p < 0.001$; for right ROI: ELECTRODE × GROUP, $F(8,404)=3.47$, $p = 0.002$]. The healthy controls had higher *alpha* power than the SA patients only in occipital sites ($p < 0.01$). Overall, *alpha* power in the resting condition was the highest in HC and the lowest in SZ, with SA having an intermediate position.

Cortical maps of SP of the *theta* and *alpha* bands are presented in Fig. 1.

In the *beta 2* band in the frontal sites [ELECTRODE × ROI × GROUP, $F(4,202) = 3.29$, $p = 0.017$] differences were only observed in ROI 2 (anterior right) [ELECTRODE × GROUP, $F(4,202) = 4.92$, $p < 0.001$]. *Beta2* power in the resting condition was the highest in SA and the lowest in SZ; with HC having an intermediate position: SA > HC in Fp2 ($p < 0.05$), in F8 ($p < 0.001$), SA > SC in F8 ($p < 0.01$), HC > SC in Fp2 ($p < 0.001$).

During the arithmetical task performance the main "GROUP" effect was only found in the *beta 2* band in the frontal sites [ELECTRODE × GROUP, $F(4.202) = 2.63$, $p = 0.039$]. In the SC patients *beta 2* power was lower than in SA in F7 and F8 ($p < 0.001$), and lower than HC in F3, F4, F7, F8 ($p < 0.05$). Compared to HC, *beta 2* power in SA was higher in F7 ($p < 0.05$) but lower in F4 ($p < 0.001$).

3.2.2. Within-group comparison of SP changes in task vs. rest conditions

In HC significant differences were found in midline sites in the *theta* band [CONDITION × ELECTRODE, $F(2,70) = 9.15$, $p = 0.005$]; the *alpha* band [CONDITION × ELECTRODE, $F(2,70) = 20.02$, $p < 0.001$]; in anterior frontal sites in the *beta 2* band [CONDITION × ELECTRODE, $F(2,78) = 4.06$, $p = 0.027$]; the *gamma* band [CONDITION, $F(1,39) = 4.51$, $p = 0.04$]; and in central/posterior parietal-occipital sites in the *alpha* band [CONDITION, $F(1,39) = 30.53$, $p < 0.001$].

In SZ, changes in SP were observed in the midline *theta* band [CONDITION, $F(1,27) = 18.2$, $p < 0.001$]; the *alpha* band [CONDITION, $F(1,27) = 17.64$, $p < 0.001$]; in the anterior frontal *theta* band [CONDITION, $F(1,31) = 5.67$, $p = 0.024$]; and *beta 2* band [CONDITION, $F(1,31) = 11.46$, $p = 0.001$]; and in central/posterior parietal-occipital sites in the *alpha* band [CONDITION, $F(1,31) = 23.29$, $p < 0.001$].

In the SA group we found changes in the midline *theta* band [CONDITION × ELECTRODE, $F(2,50) = 5.95$, $p = 0.005$]; the *alpha* band [CONDITION × ELECTRODE, $F(2,50) = 4.67$, $p = 0.028$]; anterior frontal sites in the *theta* band [CONDITION, $F(1,31)=4.26$, $p = 0.047$]; the *beta 2* band [CONDITION × ELECTRODE × ROI, $F(2,62) = 4.16$, $p = 0.025$]; the *gamma* band (on a trend level) [CONDITION × ELECTRODE × ROI, $F(2,62) = 2.98$, $p = 0.05$]; and in central/ posterior parietal-occipital sites in the *alpha* band [CONDITION, $F(1,31) = 8.54$, $p = 0.006$].

Post hoc-tests revealed an increase of midline *theta* in Fz ($p < 0.05$), and a decrease in Cz ($p < 0.001$) and Pz ($p < 0.01$) in

Table 2
ANOVA summaries of EEG spectra in midline sites.

Source	Frequency band					
	Delta	Theta	Alpha	Beta1	Beta2	Gamma
Group	$F(2,87) = 0.05$ $p = 0.95$	$F(2,87) = 0.03$ $p = 0.97$	$F(2,87) = 1.73$ $p = 0.18$	$F(2,87) = 0.63$ $p = 0.54$	$F(2,87) = 0.17$ $p = 0.84$	$F(2,87) = 1.20$ $p = 0.31$
Condition × Group	$F(2,87) = 1.07$ $p = 0.35$	$F(2,87) = 1.09$ $p = 0.34$	$F(2,87) = 1.79$ $p = 0.17$	$F(2,87) = 1.34$ $p = 0.27$	$F(2,87) = 0.08$ $p = 0.93$	$F(2,87) = 0.04$ $p = 0.96$
Electrode × Group	**$F(4.174) = 2.69$** **$p = 0.04$**	**$F(4.174) = 3.34$** **$p = 0.01$***	**$F(4.174) = 3.40$** **$p = 0.02$**	$F(4.174) = 0.92$ $p = 0.43$	$F(4.174) = 0.45$ $p = 0.72$	$F(4.174) = 0.53$ $p = 0.67$
Condition × Electrode × Group	$F(4.174) = 1.34$ $p = 0.26$	**$F(4.174) = 2.85$** **$p = 0.03$**	$F(4.174) = 2.30$ $p = 0.08$	$F(4.174) = 1.84$ $p = 0.15$	$F(4.174) = 0.47$ $p = 0.70$	$F(4.174) = 0.39$ $p = 0.78$

* Significant after Bonferroni correction for multiple comparisons ($p < .008$).

Table 3
ANOVA summaries of EEG spectra in offmidline anterior sites.

Source	Frequency band					
	Delta	Theta	Alpha	Beta1	Beta2	Gamma
Group	$F(6,198) = 0.81$ $p = 0.57$	$F(6,198) = 0.90$ $p = 0.50$	$F(6,198) = 1.04$ $p = 0.40$	$F(6,198) = 0.95$ $p = 0.46$	$F(6,198) = 1.24$ $p = 0.29$	$F(6,198) = 0.75$ $p = 0.61$
Condition × Group	$F(6,198) = 0.46$ $p = 0.84$	$F(6,198) = 0.30$ $p = 0.94$	$F(6,198) = 1.69$ $p = 0.13$	$F(6,198) = 1.53$ $p = 0.17$	**$F(6,198) = 3.19$** **$p = 0.005$***	$F(6,198) = 1.79$ $p = 0.10$
ROI × Group	$F(6,198) = 0.24$ $p = 0.96$	$F(6,198) = 0.77$ $p = 0.60$	$F(6,198) = 0.86$ $p = 0.52$	$F(6,198) = 1.26$ $p = 0.28$	**$F(6,198) = 2.31$** **$p = 0.04$**	$F(6,198) = 1.57$ $p = 0.16$
Condition × ROI × Group	$F(6,198) = 1.81$ $p = 0.09$	$F(6,198) = 2.12$ $p = 0.06$	$F(6,198) = 0.91$ $p = 0.49$	$F(6,198) = 1.03$ $p = 0.41$	$F(6,198) = 0.55$ $p = 0.77$	$F(6,198) = 0.39$ $p = 0.89$

* Significant after Bonferroni correction for multiple comparisons ($p < .008$).

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Table 4
ANOVA summaries of EEG spectra in offmidline central and posterior sites.

Source	Frequency band					
	Delta	Theta	Alpha	Beta1	Beta2	Gamma
Group	$F(10,194) = 0.50$ $p = 0.89$	$F(10,194) = 0.66$ $p = 0.76$	**$F(10,194) = 2.13$** **$p = 0.03$**	$F(10,194) = 0.51$ $p = 0.88$	$F(10,194) = 1.10$ $p = 0.36$	$F(10,194) = 0.62$ $p = 0.80$
Condition × Group	$F(10,194) = 0.79$ $p = 0.64$	$F(10,194) = 1.34$ $p = 0.21$	**$F(10,194) = 2.1$** **$p = 0.03$**	$F(10,194) = 0.87$ $p = 0.57$	$F(10,194) = 0.78$ $p = 0.65$	$F(10,194) = 0.50$ $p = 0.89$
ROI × Group	$F(10,194) = 0.95$ $p = 0.49$	$F(10,194) = 1.86$ $p = 0.05$	**$F(10,194) = 3.43$** **$p = 0.001$***	**$F(10,194) = 3.63$** **$p = 0.001$***	**$F(10,194) = 2.95$** **$p = 0.002$***	**$F(10,194) = 1.96$** **$p = 0.04$**
Condition × ROI × Group	$F(10,194) = 1.11$ $p = 0.35$	$F(10,194) = 0.74$ $p = 0.69$	$F(10,194) = 1.59$ $p = 0.11$	$F(10,194) = 0.54$ $p = 0.86$	$F(10,194) = 1.52$ $p = 0.13$	$F(10,194) = 0.69$ $p = 0.73$

* Significant after Bonferroni correction for multiple comparisons ($p < .008$).

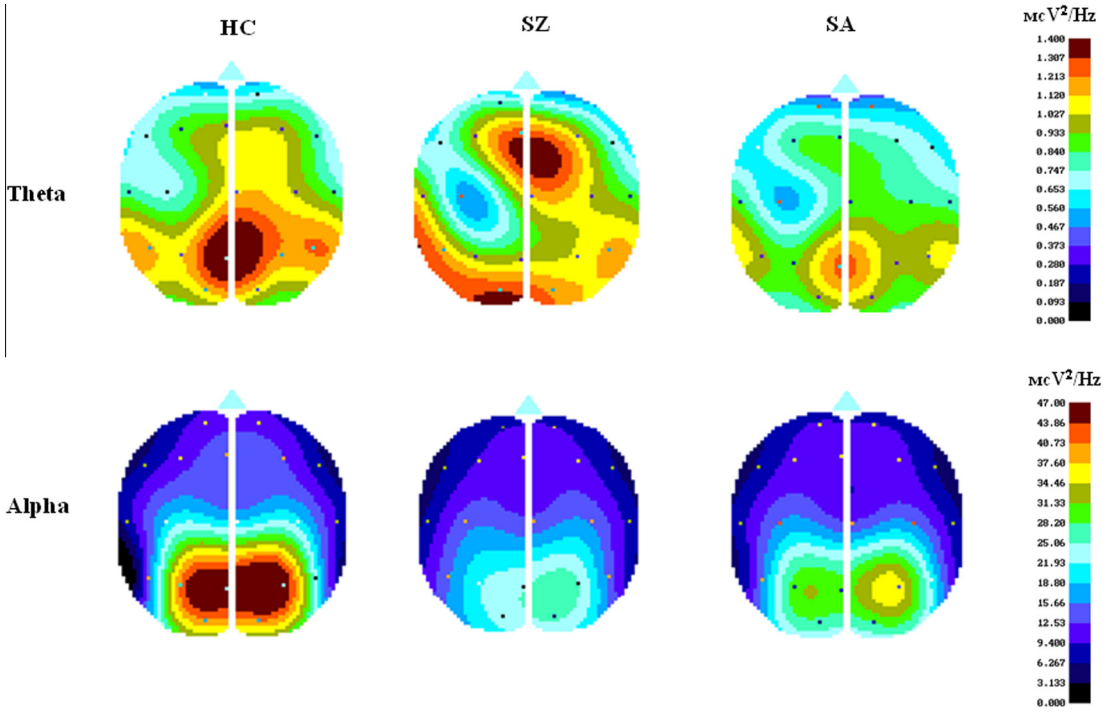

Fig. 1. Resting state theta and alpha spectral powers in healthy controls, patients with schizophrenia and schizoaffective disorder.

healthy individuals. Schizophrenia patients demonstrated a *theta* power decrease in all midline sites: Fz ($p < 0.001$), Cz ($p < 0.001$), Pz ($p < 0.001$), whereas schizoaffective patients exhibited a local decrease of *theta* power in Pz ($p < 0.001$). Moreover, SC patients demonstrated a *theta* power decrease in frontal off-midline sites: Fp2 ($p < 0.05$) and F3 ($p < 0.01$), but schizoaffective patients showed a *theta* power decrease in F4 ($p < 0.05$), F7 ($p < 0.01$) and F8 ($p < 0.05$) (Fig. 2).

Central/posterior and midline *alpha* power decreased during the in-task condition in HC in all sites ($p < 0.001$), in SZ in all sites ($p < 0.001$), and in SA in all sites ($p < 0.001$) except for Fz, Cz, T3, T4.

In off-midline anterior sites, *beta 2* power increased in Fp1 ($p < 0.01$) and decreased in F3 ($p < 0.05$) in HC, whereas in SZ there was a decrease of SP in Fp2 ($p < 0.001$), F3 ($p < 0.01$) and F4 ($p < 0.05$), SA demonstrated a decrease of SP only in left anterior ROI: Fp1, and F3 ($p < 0.05$).

In off-midline anterior sites, *gamma* power only changed in the HC and SA groups. *Gamma* power increased in all anterior sites in HC ($p < 0.01$), SA only demonstrated an increase of SP in left anterior ROI: Fp3 and F7 ($p < 0.01$). In the SZ group the *gamma* band did not significantly change (Fig. 3).

Summary of the changes of SP in task vs. rest conditions – Fig. 4.

3.3. Correlation analysis between EEG rest- and task-related parameters and PANSS scores

Significant positive correlations were obtained between SP at rest and the PANSS negative subscale sum scores in the SZ patients: in the *theta* band F4 ($r = 0.381$) and O1 ($r = 0.374$); in the *alpha* band – C3 ($r = 0.369$), C4 ($r = 0.352$), P3 ($r = 0.401$), T3 ($r = 0.357$) and Pz ($r = 0.385$); and in the *beta* band – C3 ($r = 0.384$), C4 ($r = 0.377$), P3 ($r = 0.477$), P4 ($r = 0.374$), T3 ($r = 0.419$), T6 ($r = 0.350$), Cz ($r = 0.415$) and Pz ($r = 0.530$). No correlations were found in the SA group between the PANSS scores and SP.

During the mental arithmetic task we observed significant positive correlations between SP and negative symptoms PANSS subscale in the SZ group in the *beta1* band in P3 ($r = 0.387$), F7, P3 ($r = 0.405$), T5, P3 ($r = 0.383$). In the SA patients PANSS positive subscale scores negatively correlated with the SP of the *alpha* band in C3 ($r = -0.359$), P3 ($r = -0.380$) and Pz ($r = -0.422$); *beta band1* in Fp1 ($r = -0.422$) and F7 ($r = -0.361$) and *gamma1* in Fp1 ($r = -0.368$).

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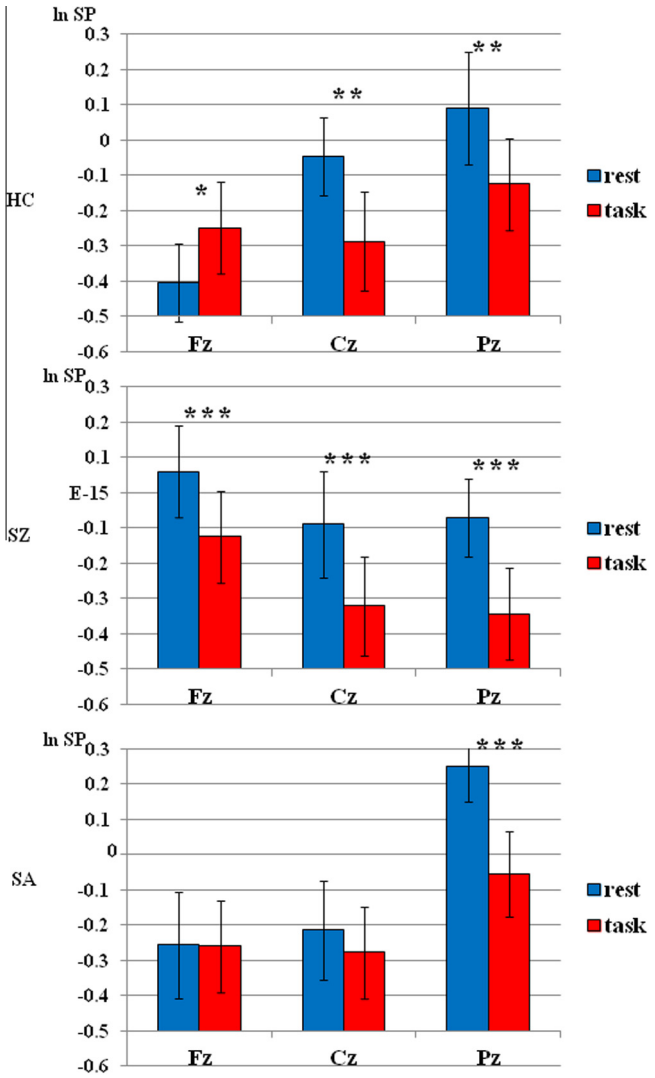

Fig. 2. Changes in midline theta SP in task vs. rest conditions.

4. Discussion

Our study had two objectives. Firstly, we investigated whether patients with schizophrenia and schizoaffective disorder with the first psychotic episode emerge with similar/ different EEG characteristics in the resting state. Secondly, assuming the distinct clinical entity of schizoaffective disorder, we tested the extent to which an implicit cognitive task can induce EEG frequency bands in these patients and how the activation of the task can differ from schizophrenia patients and healthy individuals.

The present findings underlined the previous reports of reduced alpha and increased theta frequencies in schizophrenia patients at rest (Sponheim et al., 2000; Fehr et al., 2001; Harris et al., 2006; Boutros et al., 2008; Hong et al., 2012); however, similar patterns were found in schizoaffective disorder patients. Attenuated slow frequency bands in schizophrenia patients seem to be stable across the continuum of the disease, being present in chronic and first psychotic episode patients (Sponheim et al., 1994), and they are also found in individuals at risk of psychosis (Fehr et al., 2003). However, our study did not reveal any difference in the delta band in contrast to the previous studies (Shagass, 1991). This could be due to the fact that these studies mostly included chronic schizophrenia patients, whereby emerging delta wave alterations possibly indicate progressive changes in schizophrenia. Similarly, Ranlund et al. (2014) reported an increase of the delta wave in chronic patients but not in first psychotic episode patients or in individuals with a high risk for psychosis. The increased beta2 power in the right anterior region in the resting state in both patient groups is in line with the findings of Venables et al. (2009) who also propose excessive high-frequency EEG activity over frontal brain regions as a possible endophenotype that reflects a cortical expression of genetic vulnerability to schizophrenia. Furthermore, assuming certain clinical similarities in affective states and the intermediate position between schizophrenia and healthy individuals, schizoaffective patients possess similar hemispheric patterns of high frequency bands unlike patients with depressive symptoms showing signs of right hemispheric abnormalities (Allen et al., 2004).

Additionally, we found that the severity of negative symptoms was associated to theta, alpha and beta1 bands predominantly in the resting condition in schizophrenia patients. Numerous studies suggest that theta and delta activity may be more pronounced in patients with predominant negative symptoms (see Boutros et al., 2014). In the above-mentioned study of Sponheim et al. (1994), increased theta and delta bands and a decreased alpha band were associated with negative symptoms and larger ventricles of the brain (Sponheim et al., 1994). Moreover, Gschwandtner et al. (2009) demonstrated positive correlations between negative symptoms and delta, theta, alpha 2 and beta 1 in neuroleptics-naïve first episode psychotic patients claiming that augmented slow wave power is a marker for negative symptoms in psychosis. Similar results were obtained in at-risk individuals (Zimmermann et al., 2010). One can assume that the alteration of slow frequency bands presumably occurs in all stages of the illness and seems to reflect the severity of negative symptoms. This idea goes in line with the findings of Ramos et al. (2001) who showed an association between a decreased alpha 1 band and resistance to treatment.

Increased power of the theta band and reduced alpha power have been reported as a correlate of drowsiness and transition to sleep (Matejcek, 1982) possibly due to the medication effect. We can advocate that: (1) The lack of delta rhythm alterations in our study also supports the notion that slow band alterations are not due to changes in the vigilance state (Morikawa et al., 1997); (2) Although antipsychotics may affect brain functions and contribute to the EEG abnormalities in psychotic patients, it has been also argued that such alterations have been found in unmedicated patients (Kessler and Kling, 1991; Merrin et al., 1986; Knott et al., 2000; John et al., 2003). In our study, both patient groups were medicated and medication alone does not seem to explain the differences. The similarity of their EEGs suggests that these EEG abnormalities are stable characteristics of schizophrenia and are not treatment-related epiphenomena.

From a physiological perspective the posterior alpha band at rest denotes the state of wakefulness and also reflects attentional processes. An increased resting theta band is shown to reflect attentive-like activity being carried out in the resting state (Gevins et al., 1997) and is also associated with poor verbal memory performance (Kirihara et al., 2012). Keeping in mind the intermediate position of schizoaffective patients between schizophrenia patients and healthy controls, one can assume that better cognitive performance is compensated by less attenuated baseline resting state features. Although we have no additional cognitive correlates in our study, which should be considered as a limitation, the ample evidence suggests that patients with schizoaffective disorder have less prominent cognitive deficits than schizophrenia patients (see Bora et al., 2009).

Mental arithmetic is a complex act involving various cognitive processes and is frequently used to induce a workload and investigate working memory function. It has been shown that midline

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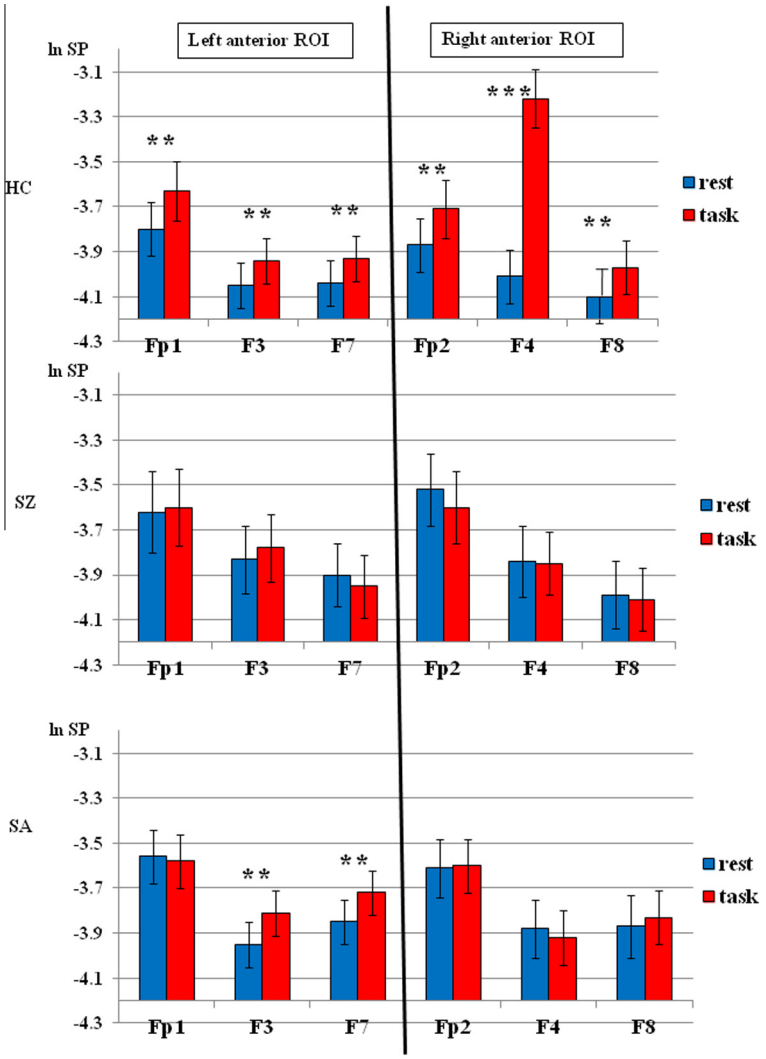

Fig. 3. Changes of anterior gamma SP in task vs. rest conditions.

theta is enhanced relative to the resting state when subjects perform complex attention demanding tasks (Gevins et al., 1997; Sammer et al., 2007). Notably, Sammer et al. (2007) found the theta power to be higher at frontal electrodes as compared to parietal electrodes. The theta increase during working memory performance can be accompanied by reduced power of the alpha band, specifically in the occipital, occipital-parietal and parietal regions (Basar et al., 2001; Klimesch, 1999; Park et al., 2011), which represent uncorrelated processes. The present evidence is supported by our current results showing that in the task performance healthy individuals exhibited an increase in midline theta power, beta 2 in the left prefrontal area and frontal gamma power with a simultaneous decrease in theta in central and parietal sites and alpha power in central, parietal and occipital areas. The increase in theta activity during task performance may be related to working memory load, with respect to the fact that the subtraction in steps of 7 is a quite difficult calculation (Klimesch et al., 1999) requiring focused attention (Gevins et al., 1997; Gundel and Wilson, 1992). With regard to the brain structures, involved in the calculation process, Dehaene et al. (2004) demonstrated that the intraparietal sulcus, the precentral and inferior prefrontal cortex are being systematically activated in calculation tasks hosting central amodal representation of quantity. Findings of the studies on arithmetical processing indicate that mental calculation is associated with increased gamma oscillations (Micheloyannis et al., 2003; Dimitriadis et al., 2012) sub-serving calculation-related attention.

In schizophrenia patients we observed a generalized decrease of midline theta power, beta 2 power in frontal areas and alpha power in central and occipital areas, whereas schizoaffective patients demonstrated a relatively local decrease in theta power in the midline parietal area, beta 2 in the left frontal region, alpha power in central and occipital areas and a local increase in the gamma band in the left frontal region. The lower level of prefrontal activation is a typical and frequent finding in schizophrenia, particularly in demanding cognitive processing (Tan et al., 2007). Correspondingly, in the fMRI study, Hugdahl et al. (2004) demonstrated that schizophrenia patients have less activation in the prefrontal regions relative to patients with depression and healthy controls. It was also shown by Elliott et al. (1997) study that abnormalities in the prefrontal activation in depression are related to the abnormal modulation of emotional behavior. In the task performance we only found a negative association between the severity of positive symptoms and the spectral power of the alpha, beta and gamma bands during the in-task condition in the schizoaffective patient group. It goes in line with the study of Omori et al. (1995) that showed a relationship between positive symptoms and higher alpha power. The failure to suppress or inhibit activity in the frontal lobes during the execution of a cognitive task may be apparent

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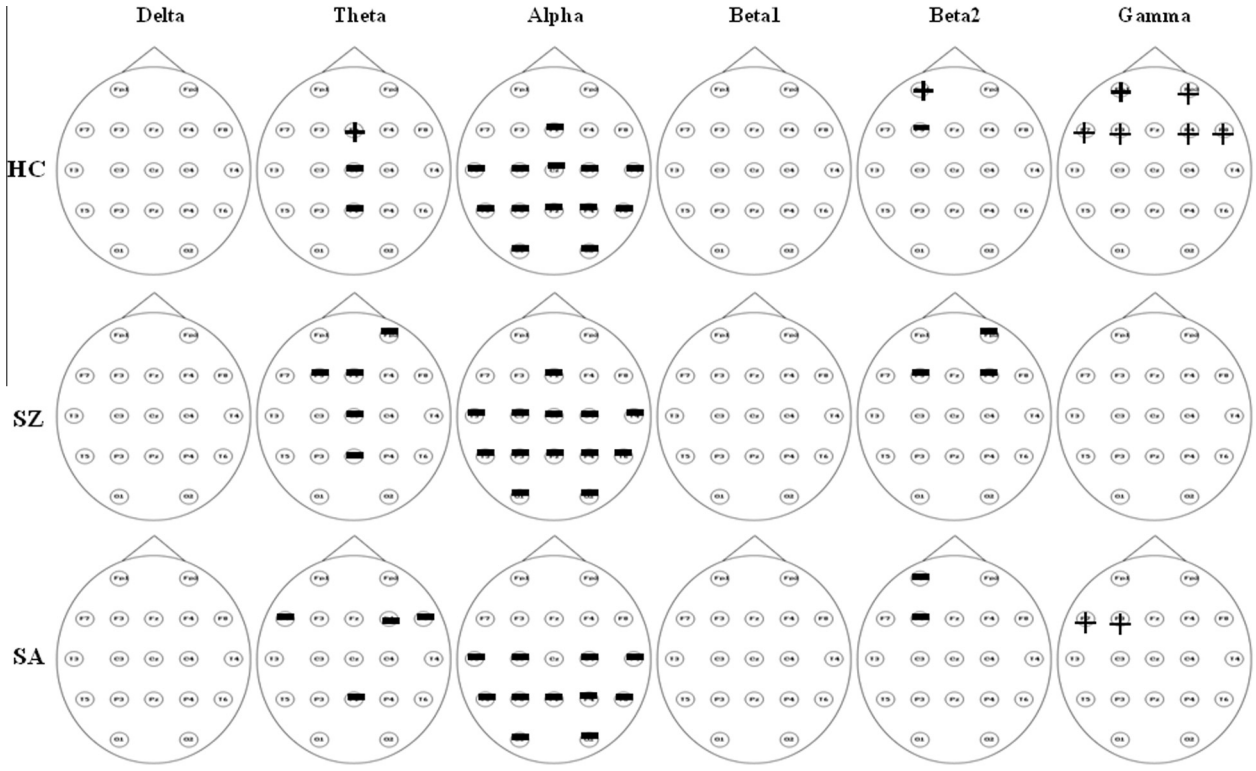

Fig. 4. Summary of the changes of SP in task vs. rest conditions. *Comment:* "+" – increase in spectral power in task vs. rest conditions; "–" – decrease in spectral power in task vs. rest conditions.

in the clinical observation that patients with schizophrenia experience problems when they are required to focus on the specific stimulus source and suppress attention to other simultaneous stimuli.

The impaired gamma band in schizophrenia patients is consistent with previous studies that applied a working memory task (Basar-Eroglu et al., 2007), and mental arithmetic task (Kissler et al., 2000), which provides further support for a relation between abnormal gamma band oscillations and the disturbance of higher cognitive processes in schizophrenia (Strelets et al., 2006). In SA during arithmetic task performance the pattern of alterations was diverse: the increased gamma band power (on a trend level) during task performance resembles the pattern of healthy individuals.

In conclusion, our results provide evidence that patients with schizophrenia and schizoaffective disorder showed similarities in EEG patterns in the resting condition, and differences in arithmetic task performance. We found no differences in behavioural performance of the mental arithmetic task, although schizophrenia patients and patients with schizoaffective disorder seem to recruit distinct brain mechanisms.

Contributors

Author Garakh participated in the design of the study, collection of data, analysis and interpretation of the results and preparation of the draft of the article. Author Zaytseva participated in the design of the study, the collection of data, the interpretation of data and drafting the article. Author Kapranova participated in collection of the data. Author Fiala participated in analysis of the data and interpretation of the results. Author Horacek participated in interpretation of the results, drafting the article. Author Shmukler participated in the design of the study, in the interpretation of the data. Author Gurovich participated in the design of the study participated in the interpretation of the data. Author Strelets participated in the interpretation of the data, and drafting the article. All authors contributed to and have approved the final manuscript.

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