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Use of Cross-Correlation Analysis of EEG Signals for Detecting Risk Level for Development of Schizophrenia

O. Yu. Panischev[1], S. A. Demin[1]*, A. Ya. Kaplan[2], and N. Yu. Varaksina[1]

Study of the cross-correlation between EEGs can be used to detect susceptibility to schizophrenia in children and adolescents (11 to 14 years old). To find diagnostic characters, we use the cross-correlation technique based on the correlation coefficient and the Fourier spectrum of the cross-correlation functions. Our findings make it possible to associate the degree of frequency–phase synchronization in a separate frequency range with risk level of development of schizophrenia.

Recent progress in clinical medicine and diagnosis provides new opportunities for mental health research. However, some mental illnesses (e.g. schizophrenia) still cannot be reliably diagnosed using laboratory tests [1]. Such illnesses are diagnosed using standard criteria based on personal interviews with the patient, while electro- and magnetoencephalography (EEG and MEG) are rarely used for diagnosis of mental illnesses [2].

Statistical methods of EEG- and MEG-processing hold considerable promise for studies of brain activity [2-5]. Earlier, such methods were reported in [3]. A decrease in the amplitude of the alpha rhythm of the EEG and an increase in the amplitude of delta and theta rhythms were demonstrated to be diagnostically significant. Low-frequency (<0.25 Hz) fluctuations of EEG signals have been observed in patients with schizophrenia [4]. EEG-based diagnostic characters for schizophrenia were reported in [5]. Signals detected by electrodes *F*3 and *F*4 were subjected to flicker-noise spectroscopy. Analysis of EEG signals of adolescents (division into four groups) allowed the susceptibility to schizophrenia to be detected.

In this work, the effect of correlation between EEG signals is discussed. The correlation between the EEG signals detected in different brain regions, as well as synchronization between cortex regions, provide information about the activity of the brain as a whole. Asynchronous or supersynchronous signals are often indicative of mental pathology [6, 7].

Basic Correlations

EEG signals were processed using a correlation coefficient widely used in mathematical statistics. The correlation coefficient between two random parameters X and Y with nonzero variation is:

$$k(X, Y) = \frac{\langle XY \rangle}{\sigma_X \sigma_Y}. \quad (1)$$

Phase–frequency synchronization is studied using the Fourier spectrum of the cross-correlation functions [7, 8]:

$$\mu_0^{XY}(\nu) = \left| \tau \sum_{j=0}^{N-1} c(t_j) \cos 2\pi\nu t_j \right|^2, \quad (2)$$

where $c(t)$ is the cross-correlation function (CCF) for two-electrode EEG signals $\{x_j\}$, $\{y_j\}$:

$$c(t) = \frac{1}{(N-m)\sigma_x \sigma_y} \sum_{j=0}^{N-m-1} \delta x_j \delta y_{j+m}, \quad t = m\tau, \quad (3)$$

where τ is sampling time constant; δx_j and δy_j are fluctuations of signals X and Y; σ_x and σ_y are mean-square deviations:

[1] Institute of Physics, Kazan Federal University, Kazan, Russia; E-mail: serge_demin@mail.ru
[2] Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia.
* To whom correspondence should be addressed.

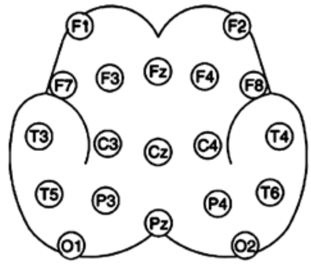

Fig. 1. International 10-20 scheme of EEG electrode positioning.

$$\delta a_j = a_j - \langle A \rangle; \quad \langle A \rangle = \frac{1}{N}\sum_{j=0}^{N-1} a_j;$$

$$\sigma_a = \sqrt{\frac{1}{N}\sum_{j=0}^{N-1} \delta a_j^2}; \quad a = x, y; \quad A = X, Y.$$

The Fourier spectrum of the CCF (2) is the power spectrum with respect to frequency. In the case of the autocorrelation function, the quasi-periodic frequency can be obtained. The Fourier spectrum of the CCF represents coordination/discoordination of signals at a given frequency. The synchronization effect is manifested as splashes at the given frequency. Discoordination between individual brain segments is a diagnostic symptom of certain mental diseases [5-7]. The use of MEG in such diagnosis was reported in [6, 7]. In the case of photosensitive epilepsy, the frequency 50 Hz was found to be indicative (for some sensors, an additional component at 100 Hz was also observed).

Experimental Results

EEG signals were detected using the standard 16-electrode scheme (*O*1, *O*2, *P*3, *P*4, *Pz*, *T*5, *T*6, *C*3, *C*4, *Cz*, *T*3, *T*4, *F*3, *F*4, *F*7, *F*8) installed using standard 10-20 pattern (Fig. 1). The experiments were carried out at the Mental Health Research Center (MHRC), Russian Academy of Medical Sciences, using the BrainAmp apparatus (Brain Products GmbH, Germany). The patients were relaxed with closed eyes. The EEG record time was 1-2 min. Sampling frequency was 128 Hz (methods are described in more detail in [2-4]). A total of 84 children and adolescents (including 45 patients with schizophrenia) were tested. The diagnosis was corroborated by physicians from MHRC. The control group consisted of 39 healthy subjects. Each patient was encoded by a 2/3-digit number. Prefix "S" was used for control group.

Discussion

The diagnostic characters of schizophrenia were determined through the following stages:

1) Electrode combination with maximal divergence in two groups of patients. The correlation coefficient was calculated from Eq. (1). The number of combinations for 16 electrodes was determined for the groups of patients:

$$C_n^k = N \cdot \frac{n!}{k!(n-k)!},$$

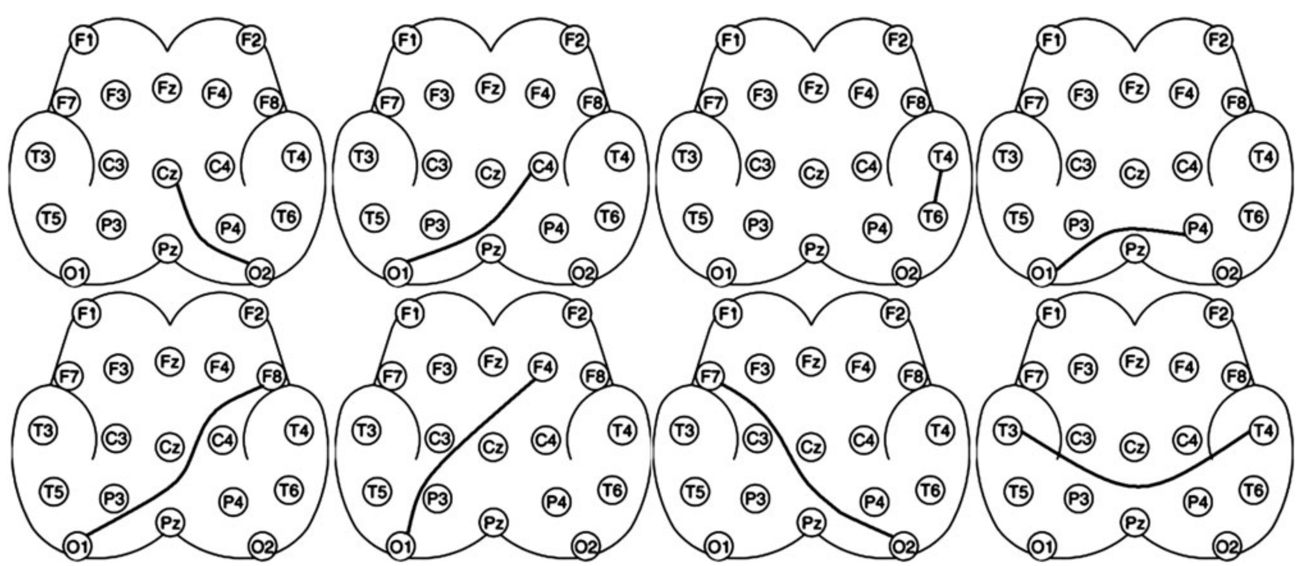

Fig. 2. Most significant deviations in correlation coefficients for pairs of electrodes.

TABLE 1. General Results of the Diagnostic Method

Subject	Diagnosis	Subject	Diagnosis	Subject	Diagnosis	Subject	Diagnosis
S10	CN	S154	CN	425	CP	401	CP
S12	CN	S155	CN	022	CP	423	CP
S18	CN	S157	CN	032	CP	429	CP
S20	CN	S158	CN	033	CP	454	CP
S26	CN	S163	CN	088	CP	485	CP
S27	CN	S164	CN	103	CP	508	FN
S31	CN	S165	CN	113	CP	509	CP
S42	CN	S167	CN	155	CP	510	FN
S43	CN	S169	CN	156	FN	515	CP
S47	CN	S170	CN	192	CP	517	CP
S50	FP	S173	CN	219	CP	540	FN
S53	CN	S174	FP	221	CP	548	FN
S55	CN	S176	FP	249	CP	573	CP
S59	CN	S177	CN	276	CP	575	FN
S60	CN	S178	FP	307	CP	585	CP
S72	CN	S179	CN	312	FN	586	CP
S78	CN	S182	CN	314	CP	642	CP
S85	CN	S196	FP	342	FN	683	CP
S94	CN	083	FN	382	CP	719	CP
S152	FP	084	CP	387_02	CP	229	FN
S153	CN	351	FN	387_03	CP	416	CP

CP	0	1	18	15
CN	19	14	0	0
FP	2	4	0	0
LN	0	2	3	6

where N is total number of patients; n is number of EEG electrodes; k is number of EEG electrodes per combination. Thus, the correlation coefficient was determined for 10,080 combinations of EEG electrodes.

The results obtained in each electrode combination were averaged over groups. Pairs of electrodes corresponding to maximal deviation were found using the correlation method. Eight pairs of electrodes with mean correlation coefficients differing 2-3-fold were detected (Fig. 2). It should be noted that deviation in other cases was 1.5.

2) Phase–frequency synchronization was tested using the Fourier spectrum of the cross-correlation functions for significant electrodes.

The CCF power spectrum for a pair of electrodes was considered as an example of such analysis. The EEG records of two patients were discussed. The CCF power spectrum recorded using electrodes $O1$ (occipital region) and $F4$ (frontal region) are shown in Fig. 3a for patient S47 of the control group. Maximal amplitude splash was observed at frequency 10 Hz (alpha rhythm in EEG of waking patients with closed eyes). Another EEG pattern was observed in patient 113 (Fig. 3b). Maximal amplitude splash was observed at frequency 10 Hz.

Analysis of the aggregate of power spectra ($84 \times 8 = 672$) demonstrated that the frequency range for healthy subjects was 8-12 Hz, whereas in patients with schizophrenia it was 0.2-2.5 Hz. Thus, synchronization at frequency 0.2-2.5 Hz in 5 of 8 pairs of electrodes is an indication of schizophrenia.

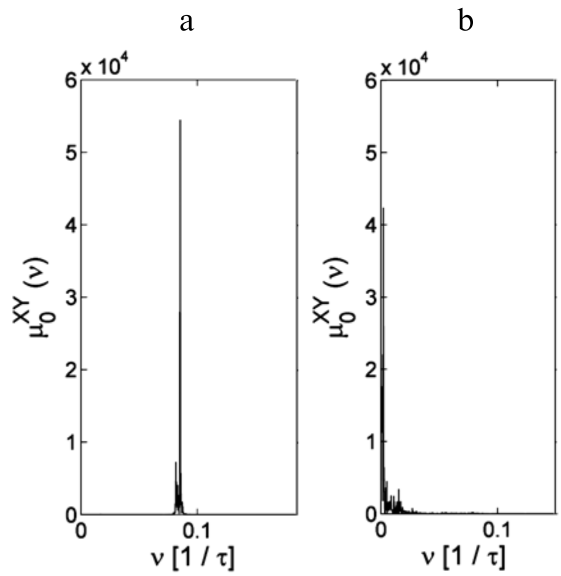

Fig. 3. Power spectra of CCF for EEG signals detected by electrodes *O*1 and *F*4 in apparently healthy subject S47 and patient 113: a) healthy subject S47, group 1; b) patient 113, group 2.

General results obtained using the method for diagnosis of susceptibility to schizophrenia suggested in this work are given in Table 1. These results were compared with the conclusions made on the basis of examinations performed at MHRC [2-4]. The method described above (5 of 8 pairs of active electrodes) was used in the diagnosis.

The following notation was used to describe the results of diagnosis: CP – confident positive (diagnosis was supported clinically); CN – confident negative (negative diagnosis was supported clinically); FP – false positive (the stated diagnosis was not supported clinically); FN – false negative (negative diagnosis was not supported clinically).

The efficiency of schizophrenia diagnosis was determined:

– sensitivity (S), %: 76;
– specificity (Sp), %: 85;
– overall accuracy (TA), %: 80;
– error probability in negative diagnosis (NP), %: 15;
– error probability in positive diagnosis (PP), %: 24.

The following equation derived in [9] was used in calculations:

$$S = [CP/(CP + FN)]\cdot 100\%;$$

$$Sp = [CN/(CN + FP)]\cdot 100\%;$$

$$TA = [(CP + CN)/(CP + FN + CN + FP)]\cdot 100\%;$$

$$NP = [FP/(CN + FP)]\cdot 100\%;$$

$$PP = [FN/(CP + FN)]\cdot 100\%;$$

Conclusion

The analysis of clinical EEG data can be used in diagnosis of susceptibility to schizophrenia in children and adolescents (11 to 14 years old). To find the diagnostic value, we use the cross-correlation technique based on the correlation coefficient and the Fourier spectrum of the cross-correlation functions (power spectra). The low-frequency (0.2-2.5 Hz) dynamics of the EEG signals was found to be typical of children and adolescents with schizophrenia. In the control group, synchronization at 8-12 Hz is observed. The phase–frequency synchronization observed in CCF spectra can be considered as a criterion for more accurate diagnosis of susceptibility to schizophrenia.

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