

Surface EMG Parameters in Schizophrenia Patients*

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Abstract—The aim of the study was to compare a variety of surface EMG (sEMG) parameters in several groups of schizophrenia (SZ, n=69) patients and healthy controls (n=44). We computed spectral, mutual information (MI) based and recurrence quantification analysis (RQA) parameters of sEMG. The major finding is that sEMG of the controls had higher values of the MI-based parameter, mean and median spectrum frequencies, and lower values of most of RQA parameters. It means higher content of recurrent fragments in sEMG of SZ patients. We suggest that the differences might be caused by either denervation/renervation process of single muscle fibers in SZ patients and/or by increased motor unit synchronization induced by antipsychotic therapy.

I. INTRODUCTION

Schizophrenia (SZ) is one of the most socially significant neuropsychiatric diseases. About 1% of population suffers from schizophrenia, regardless of the development level of a country. According to the plausible current hypothesis, SZ symptoms are linked with increased dopamine production in mesocortical and mesolimbic pathways and increased density of D2-receptors [1]. Dopamine receptors play an important part in muscle tone regulation [2], so it is likely that hyperproduction of dopamine and increased sensitivity of dopamine receptors in schizophrenia can affect not only mental processes, but also electromyogram (EMG).

Earlier studies have shown that SZ is characterized by a set of motor dysfunctions. Among them are abnormal motor development and muscle hypotonia in preschizophrenic infants [3], ataxia, extrapyramidal disturbances, pathological locomotor patterns [4], dyskinesia [5], asymmetry of motoneurons excitability [6], reduced ability to motor reorganization, and disrupted neural plasticity [7]. Whatmore and Ellits [8] have demonstrated an increased motor activity and sEMG amplitude in SZ patients coined as "hyperponesis".

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Crayton et al. [9] have revealed increased muscle fiber density and number of single muscle fiber action potentials belonging to the same motor unit (MU) thus evidencing denervation/reinnervation process in psychosis patients. Gait of schizophrenic children is slower than that of normal ones and has shorter muscle activity at both stance and swing phases [10]. Flyckt et al. [11] have revealed in SZ patients pathologically increased amplitude of MU potentials, which nonetheless did not correlate with muscle biopsy findings.

Interestingly, in Parkinson's disease (PD), which is characterized by the dopamine deficiency in the basal ganglia, surface sEMG (sEMG) contains large portions of clustered potentials. This causes specific changes in many of sEMG parameters, e.g. decreased entropy and correlation dimension, and increased determinism. sEMG in PD in a way is more predictable, less complex and more regular. [12], [13] In this study, we hypothesized that increased release of dopamine in SZ may cause changes in sEMG, which are opposite to those of PD patients. Therefore, the aim of the present study was to compare a variety of sEMG parameters in several groups of SZ patients and healthy controls. We divided all SZ patients in two subgroups: SZ patients in the remission phase (SZ-R) and patients in acute psychosis (SZ-AP). The latter was further subdivided into patients with catatonia (SZ-AP/K) and drug-naïve patients who had never taken antipsychotics (SZ-AP/APN).

II. PATIENTS AND METHODS

A. PATIENTS

SZ-AP group (n=63) included SZ-AP/APN (n=11) and SZ-AP/K (n=8). These patients were examined in the Republic Mental Hospital (settlement Matrosy, Republic of Karelia, Russian Federation). SZ-R group (n=16) was examined in the Republic Psychoneurologic Dispensary (Petrozavodsk, Republic of Karelia). 10 of the patients were later excluded from the analysis. A variety of symptoms, such as delusions, hallucinations, psychomotor stupor or agitation, disorganized behavior, and absence of criticism of pathological experience were characteristic for all patients under psychotic condition. Duration of psychosis by examination ranged from several days to several weeks. Catatonia in the SZ-AP/K group mainly appeared in the form of substupor with lethargy, catalepsy, mutism, and usually it was combined with delusions or hallucinations. Examination of antipsychotic-naïve patients as a separate group (SZ-AP/APN) seems to be a relevant model to investigate the disease *per se*, and to evaluate the action of antipsychotic medication.

The SZ-R group was formed of patients without psychotic deterioration for at least 6 months. Patients who had organic brain lesions beside schizophrenia (traumatic brain injury, neuroinfections, alcoholism, substance dependencies, and vascular brain diseases) were excluded from the study, as well as the patients who were taking psychotropic drugs beside antipsychotics (antidepressants, mood-stabilizing drugs) or drug-induced parkinsonism correctors such as trihexyphenidyl. Taking of benzodiazepine tranquilizers was accepted not less than 15 hours before examination. A control group (Con, n=44) was formed of mentally and physically healthy age- and sex-matched subjects (18 to 58 years).

The study was approved by the ethical committee of the Republic Mental Hospital (decision #8, 4/11/2012). The written informed consents were obtained from all patients and healthy control subjects.

B. METHODS

sEMG was measured in standing position from *m. biceps brachii*, with a forearm flexed at 90° (parallel to floor) without any load. Prior to electrode placement, the skin was carefully cleaned and appraised with cotton alcohol swab. A bipolar electrode with inter-electrode distance of 15 mm was used. The reference electrode was attached to ipsilateral wrist. Records were performed with Neuro-MVP 4 (NeuroSoft Inc., Ivanovo, Russian Federation) at sampling frequency 20 kHz with 50 Hz notch filter enabled. Each record was 1 s (20001 samples) long. Data processing and analysis, with the exception of mutual information calculations, were performed with Matlab software (MathWorks Inc., Natic, USA). Mutual information was computed using program by E. Weeks (USA) [14].

During preliminary visual check of sEMG spectra, sharp peaks at frequencies multiple of 50 Hz (harmonics) were found in some records, what means power line interference. We excluded from analysis those records for which the share of the harmonics in total signal power was greater than 6.8% (5 of Con, 2 of SZ-R, 8 of SZ-AP, including 1 of SZ-AP/K and 1 of SZ-AP/APN). This critical value (6.8%) was computed using sEMG records from 20 healthy subjects, who were not included in the Con group. Additionally, Fourier interpolation was applied to sEMG records [15]. Namely, amplitudes at frequencies multiple of 50 Hz were replaced by linearly interpolated values, calculated from two adjacent points. Also, all amplitudes for frequencies higher than 399 Hz were replaced by zeroes in frequency domain. Then the signals were detrended with smoothness priors method ($\lambda = 10^5$, attenuation at 10 Hz is -40 dB) to remove possible movement artifacts [16].

Among spectral measures, mean and median frequencies (MNF and MDF) of power spectra were computed.

Then, a phase space embedding was performed, i.e. signal values $\{x_1, x_2, \dots, x_n\}$ were replaced by vectors X_i (1) in m -dimensional space, with L being the time lag.

$$X_i = (x_i, x_{i+L}, x_{i+2L}, \dots, x_{i+(m-1)L}) \quad (1)$$

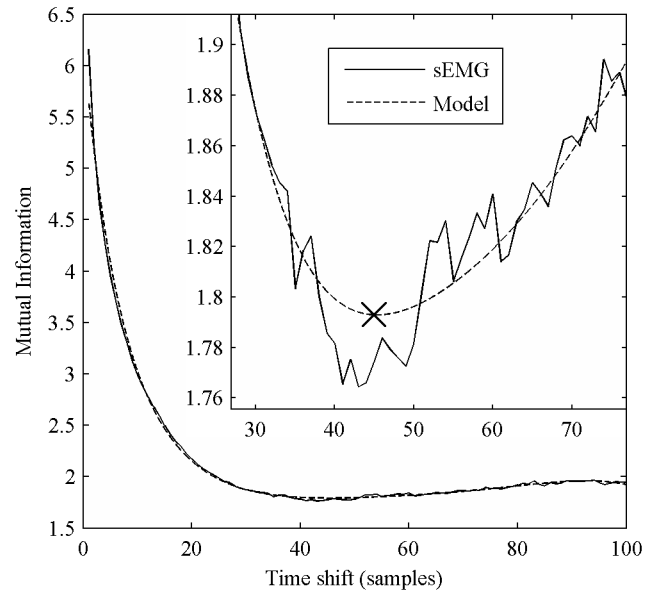


Fig. 1. Smoothing of dependence of mutual information on time shift to find the first minimum (black cross)

If m and L values are correct, X_i values make up a smooth trajectory in \mathbb{R}^m space, which corresponds to the dynamics of the examined system. Mathematical justification of this procedure is the embedding theorem by Takens-Mañé [19], [20]. For each record an optimal delay T_j was determined as first minimum of dependence $I(\tau)$, where I is mutual information of a signal and the same signal shifted backwards in time, and τ is the time shift [21], [22]. $I(\tau)$ was calculated for τ from 1 to 100 using the program of E. Weeks [14] and smoothed by least squares fitting of a model curve $I_m(\tau)$ (2) with coefficients c_0 - c_6 being fitted, then first integer minimum T_j of the fitted curve was found (Fig. 1).

$$I_m = \exp(c_0 + c_1\tau + c_2\tau^2 + c_3\tau^3 + c_4\tau^4 + c_5\tau^5 + c_6\tau^6) \quad (2)$$

L was chosen as rounded average of all T_j . Dimension m was chosen with help of false nearest neighbors (FNN) method [22], [23]. For each record, number of FNNs was calculated for m from 1 to 15, and normalized by number of FNNs for $m=1$ multiplied by 100%. Then, for each m a maximum percentage of FNNs was found among all records. Minimal m for which this maximum percentage did not exceed 1% was chosen as the embedding dimension ($m=5$).

Approximate entropy (ApEn) [17] was computed with tolerance distance $r = 0.2 * std(x)$. Sample entropy (SampEn) [18] was computed as approximate entropy with uncounted self-matches and $r = 0.481 * std(x)$, which was the minimum r allowing to avoid $\ln(0)$ for all the records. We used lag L and Euclidian distance in ApEn and SampEn computations.

Further analysis was performed by means of recurrence plots [24]. Recurrence plot R is a matrix of size $N \times N$, where N is the number of trajectory points. Matrix element at the crossing of a column and a row is equal to one, if the points corresponding to the column and the row are not further apart from each other than ε , and is equal to zero

otherwise (3), where $i, j = 1 \dots N$, $\Theta(\bullet)$ is the Heaviside function, $\|X\|$ is Euclidian norm. ε was found to be optimal at approximately $0.117 * \max(\|X_i - X_j\|)$.

$$R_{i,j} = \Theta(\varepsilon - \|X_i - X_j\|) \quad (3)$$

Recurrence plot makes it possible to analyze how often and for how long time a system returns to its previous states. Pairs of points with index difference $W \leq 375$ were not considered, so recurrence plots included white strip along main diagonal. Two examples of the obtained recurrence plots are presented on Fig. 2. Recurrence quantification analysis (RQA) of the recurrence plots was performed. We calculated recurrence rate RR, determinism DET, laminarity LAM, $\text{RATIO} = \text{DET}/\text{RR}$, average diagonal line length L, trapping time TT, maximum diagonal line length L_{\max} , maximum vertical line length V_{\max} , divergence DIV, entropy ENTR, and TREND [11]. Parameters l_{\min} and v_{\min} required to calculate DET, LAM, L, and TT were fitted to maximize the variance of DET and LAM ($l_{\min} = 25$, $v_{\min} = 50$). Parameter \tilde{N} required for measure TREND was chosen as $N - 10$ ($\tilde{N} = 19811$).

Computed parameters were compared using Kruskal-Wallis test in Matlab. The SZ-AP and SZ-R groups were compared with the Con group and with each other. The SZ-AP/K group was compared with the group of non-catatonic patients (SZ-AP/NK). The SZ-AP/APN group was compared with the group of non-antipsychotic-naïve patients (SZ-AP/NAPN) and with the Con group.

III. RESULTS

The major result is that the group of healthy controls was clearly different from the whole group of SZ patients. Namely, sEMG of the Con group had higher values of MNF, MDF, DIV and lower values of T and most (7 out of 11, $p < 0.05$) of RQA parameters in comparison with the SZ-AP group (see the group median values in Table I). In a whole, sEMG records of the SZ patients were characterized by higher determinism ($\approx 56\%$) than those of the healthy controls ($\approx 35\%$). Interestingly, according to DET, LAM, L, L_{\max} , DIV parameters, the SZ-R group was positioned between the healthy controls and patients in acute psychosis. This forms a kind of continuum of states from a non-SZ state to a severe SZ state. There were no significant differences between the SZ-AP and SZ-R groups; between the SZ-AP/K and SZ-AP/NK groups; between the SZ-AP/APN and Con groups. ApEn, SampEn, RR, RATIO, TREND parameters never showed any significant differences, so they are not included in Table I.

IV. DISCUSSION

According to our original hypothesis, increased dopamine production in SZ patients would cause changes in sEMG strictly opposite to those in PD patients. As such, determinism of sEMG signal in SZ patients should decrease, but that was not the case. Instead, we found that parameters, which estimate determinism in different ways, were increased in all SZ patients. It means higher content of recurrent fragments

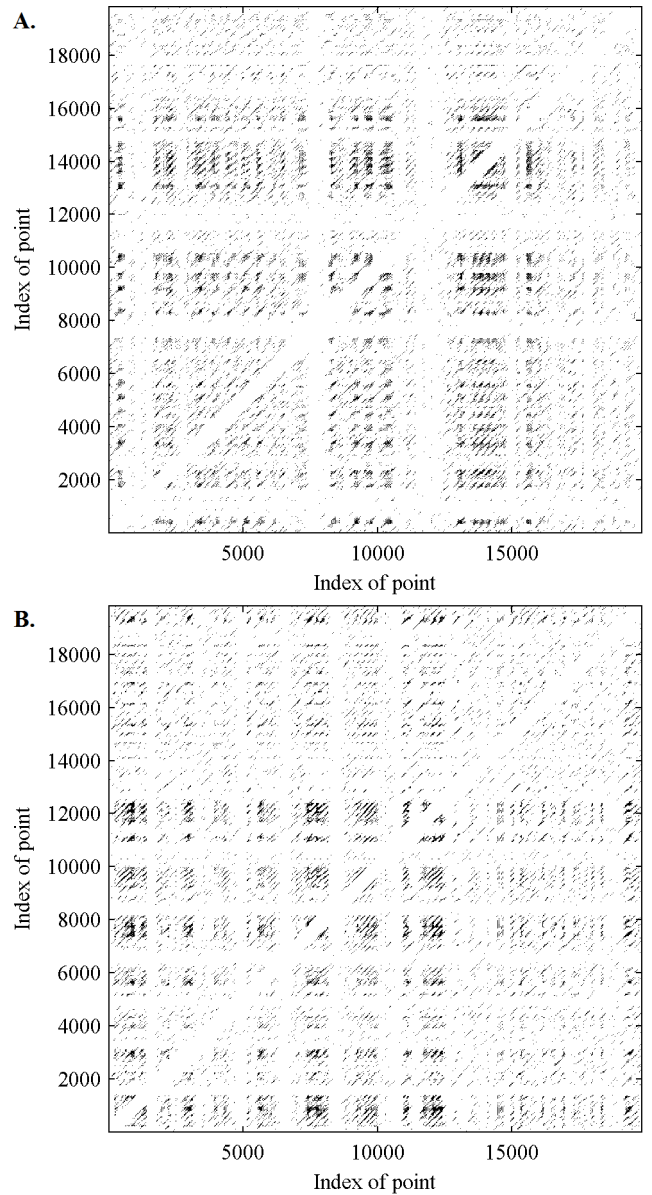


Fig. 2. Recurrence plots of sEMG: A. A subject of Con group ($RR = 4.46\%$, $DET = 35.4\%$) B. A subject of SZ-AP group ($RR = 4.04\%$, $DET = 46.6\%$)

in sEMG of SZ patients in comparison to healthy controls. This is similar to sEMG of PD patients [12]. It could well be related to the effect of the antipsychotic therapy, which might have caused drug-induced parkinsonism [25]. It is supported by the fact that DET% of the drug-naïve SZ patients was lower than that of the other SZ patients. In a whole, medication (anti-psychotic therapy) has a PD-like effect on sEMG in SZ patients. This is in a good line with a newly elaborated dopaminergic deficit hypothesis of SZ, which is opposite to the conventional dopamine hyperactivity hypothesis of SZ [26].

On the other hand, SZ *per se* has its own effect on sEMG, because most of sEMG parameters in the drug-naïve group (SZ-AP/APN) were still different from the Con group,

TABLE I
INTERGROUP COMPARISONS OF SEMG PARAMETERS

Group	Parameter										
	MNF(Hz)	MDF(Hz)	T	DET	LAM	L	TT	L _{max}	V _{max}	DIV	ENTR
Con	129	113	38	0.354	0.220	47.7	75.4	406	311	2.46E-03	3.99
SZ-R	112*	97**	47**	0.382	0.229	48.8	73.8	412	310	2.43E-03	3.99
SZ-AP	118**	104**	43***	0.562**	0.387**	54.8**	84.7*	502*	443**	1.99E-03*	4.19**
SZ-AP/NAPN	116	102	44	0.572	0.406	55.3	85.6	512	452	1.95E-03	4.22
SZ-AP/APN	129*	115*	39**	0.429	0.282	50.0	80.7	423	368	2.38E-03	4.05
SZ-AP/K	107	95	51	0.570	0.430	55.7	94.9	517	713	1.93E-03	4.20
SZ-AP/NK	118	104	43	0.554	0.346	53.5	82.7	497	436	2.01E-03	4.19

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Values are medians of sEMG parameters of the groups. Comparisons are between the SZ-R and Con groups; between the SZ-AP and Con groups; between the SZ-AP/APN and SZ-AP/NAPN groups. T unit is the number of sampling periods. ENTR unit is bit.

though statistically insignificantly. More precisely, median sEMG parameters of the SZ-AP/APN group, excepting MNF and MDF, were positioned between those of the Con and SZ-AP groups. We suppose, that changes in the level of MUs and/or muscle fibers might be a prerequisite to observed sEMG data due to well documented denervation/renervation in SZ patients [9]. Denervation and further sprouting causes "giant" (up to 1000 μ V) MU potentials, which may manifest itself as higher rhythmicity of sEMG [27].

In conclusion, we found that most of sEMG parameters in the presented group of SZ patients were clearly different from the control group. We believe, that coupling of the clinical data from SZ patients with sEMG parameters would be helpful in further understanding of motor symptoms and sEMG changes in SZ patients. Also, a study of MU impulsing activity and modeling of sEMG in SZ patients would be essential.

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