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## Study of changes in the characteristics of physiological signals after orthodontic treatment

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This paper examines the effect of orthodontic correction on the characteristics of the EEG signal obtained during a cognitive test. This approach allows us to find differences for different groups of patients (with different strengths of orthodontic influence) after treatment and will help in the future to monitor the condition of patients for treatment adjustment. The work showed that EEG characteristics differ most strongly for some effects immediately after the intervention, and for others a long time after it.

**Keywords:** electroencephalography, recurrent analysis, living systems, inclusion.

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The problems of inclusion are now becoming more and more apparent in long-term therapy [1]. Orthodontic correction with braces or aligners is one such type of treatment [2]. The placement and wearing of such devices may cause long-term discomfort and problems of various kinds. It has already been demonstrated in certain studies that pain and stress are detrimental to cognition [3]. This is the reason why EEG signal characteristics obtained in the course of cognitive testing are proposed to be analyzed in the present study.

Recurrent analysis, which is used below to examine EEG records, appears to be suitable for processing of complex signals, since the method itself, in contrast to many other more traditional techniques for frequency analysis, is easy to implement and is not computationally intensive [4]. In addition, recurrent analysis remains applicable to any type of physiological data without the need to alter the method in any significant way [5–7]. This may prove useful in further studies into the effect of orthodontic treatment on other biological signals. The statistical stability of recurrence measures [8], which provides an opportunity to work even with small samples, is also an important factor of applicability of recurrent analysis to physiological records.

In the present study, the following experimental procedure was proposed for a thorough investigation of the effect of orthodontic treatment on the condition of a patient: the first record was made two weeks prior to orthodontic correction with braces or aligners, the second experiment was performed immediately after orthodontic correction, and the third experiment was carried out two weeks after that.

The experiment itself was a sequence of four cognitive tests (Fig. 1). In the first test, participants are required to press on circles in the order of decreasing numbers from 25

to 1. When pressed correctly, circles vanished, simplifying the task in the course of testing. The second test is a task on remembering the positions of dots in a square field of 16 cells. A patient needs to remember the presented configuration of dots and reproduce it in a blank field on a pad. The third test involves the use of Schulte tables. It is similar to the first one, but the complexity of a Schulte test does not change during testing [9,10]. The fourth test is a counting task. A patient is presented with a certain number of intersecting squares, and he should tell whether this number was odd or even.

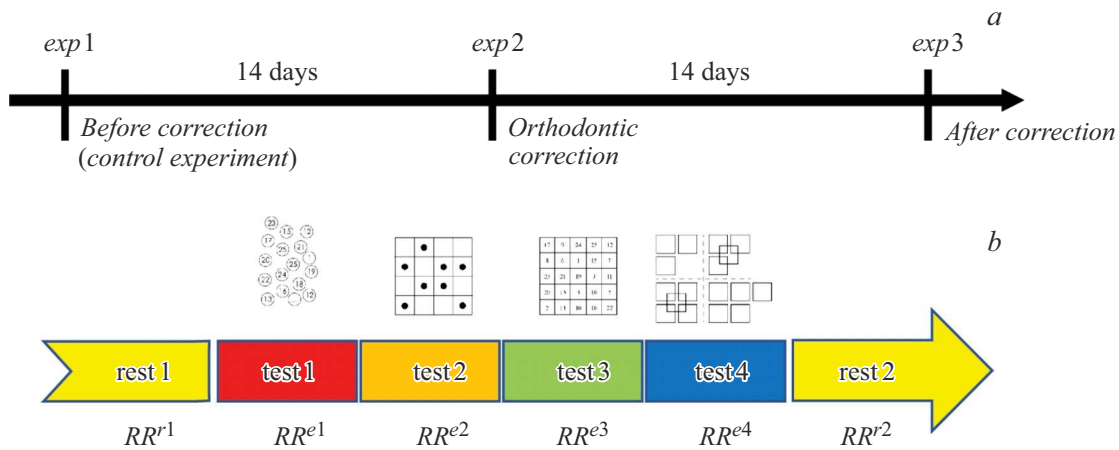
The brain electrical activity was recorded in the standard 10-20 system [11]. At the start and end of recording, a patient was asked to rest for five minutes with eyes closed.

As was already mentioned, recurrent analysis was used to process EEG data. This method is applied in a wide range of processing tasks involving complex signals of various nature [12]. The calculation algorithm itself is notable for its simplicity [13], which makes it promising for application to big data and real-time signal processing. Let us examine signal  $x(t)$  with its values known at time points  $t_i$ , where  $i = 1, \dots, n$ . A recurrence matrix may be constructed for it in the following way:

$$R_{ij} = \theta(\varepsilon - \|x(t_i) - x(t_j)\|), \quad (1)$$

where  $R_{ij}$  is the recurrence matrix element for signal  $x(t)$ ;  $t_i$  and  $t_j$  are moments of time  $t$ ;  $\varepsilon$  is the empirically determined threshold ensuring the needed accuracy of the method; and  $\theta(\dots)$  is the Heaviside step function that assumes a value of 0 for negative arguments and 1 for non-negative arguments:

$$\theta(z) = \begin{cases} 0, & z < 0, \\ 1, & z \geq 0. \end{cases} \quad (2)$$



**Figure 1.** Diagrams of experimental sessions (a) and each experiment (b).  $RR^k$  — recurrence measures for the corresponding time intervals.

Thus, a recurrence matrix constructed in accordance with expressions (1) and (2) is formed from two types of elements: „0“ and „1“. A matrix element is equal to „1“ if signal value  $x(t_i)$  at time point  $t_i$  falls within the  $\varepsilon$ -neighbourhood of signal value  $x(t_j)$  at time point  $t_j$ . At the same time, a matrix element is equal to „0“ if the values of signal  $x$  at time points  $t_i$  and  $t_j$  lie far from each other. Recurrent matrices (1) are often presented graphically in the form of recurrence plots with dots representing unit values and blank pixels corresponding to zero values. Thus, the recurrent properties of time series  $x(t_i)$  are presented in the form of geometric structures and allow one to visualize the dynamics of a series as a simple graphical convolution.

Recurrent analysis incorporates the methods for examination of dot positioning on the recurrence plot surface, which were used in recent years to process stochastic time series of various nature. Note that a structure similar to a lattice with its period corresponding to the oscillation period of a system forms in a recurrence plot in the case of single-frequency periodic dynamics. The higher the number of repetitions of a certain value is, the greater is the number of elements of a recurrence matrix equal to „1“. It is then easy to deduce that the number of dots in a recurrence plot increased with oscillation frequency (if all the other parameters remain unchanged). This fact allows one to identify readily the most frequent values in a signal.

In the course of experiments (see Fig. 1), two records were made in a state of rest, and a single record was made in each of the four cognitive tests. Thus, six natural time intervals allowing one to estimate the recurrence measure were recorded. The recurrence measure formula for each time interval  $k$  then takes the following form:

$$RR^k = \frac{1}{(t_k^f - t_k^s)^2} \sum_{i=t_k^s}^{t_k^f} \sum_{j=t_k^s}^{t_k^f} R_{ij}. \quad (3)$$

A specific window width was chosen for each record of each patient depending on the experiment duration. These

widths vary from patient to patient and from test to test, but this drawback is mitigated by normalization to the series length in calculation of the recurrence measure. This provides an opportunity to evaluate the temporal variation of the recurrence measure and determine which values correspond to different cognitive tests and periods of rest.

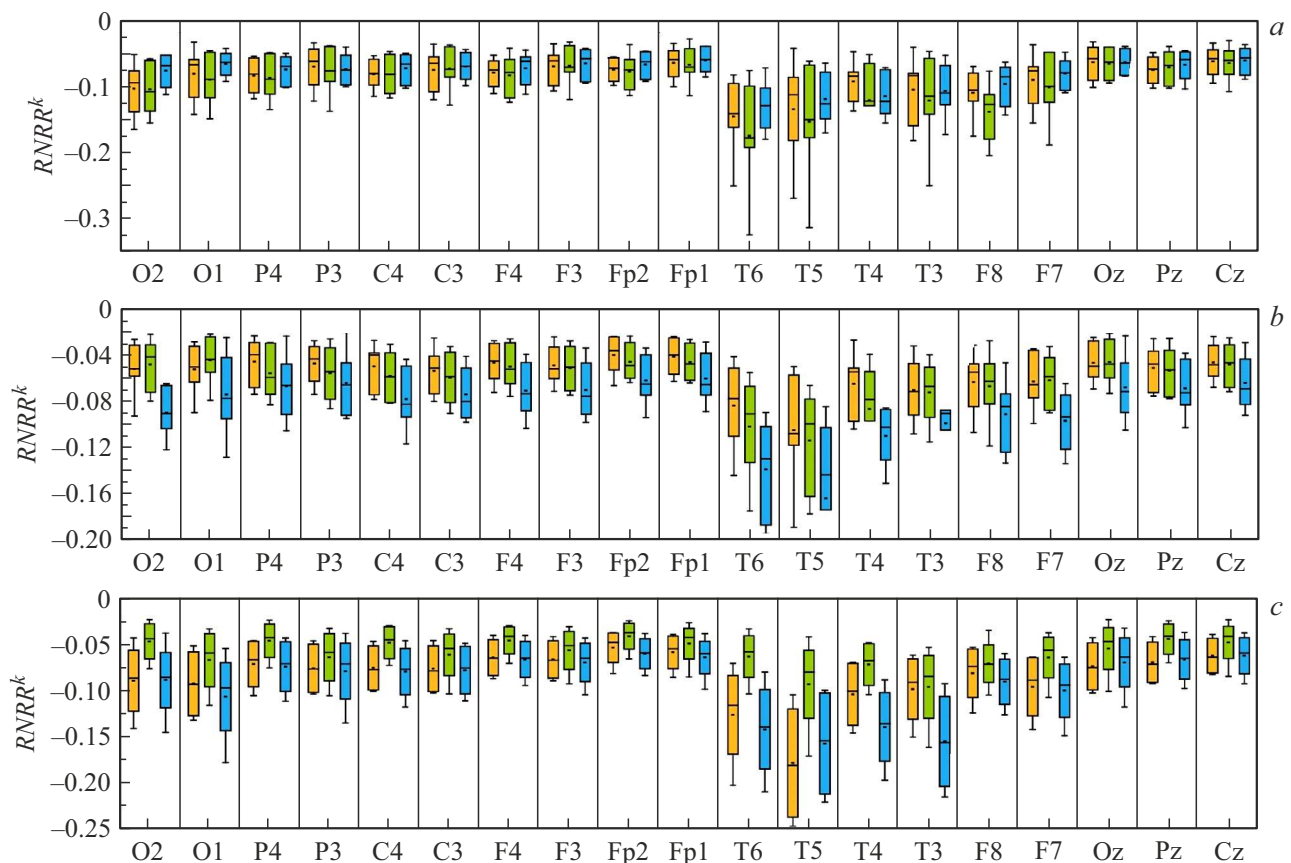
Since the deepest relaxation is achieved in a state of rest, which is closer to the natural state of a patient, it appears reasonable to normalize the recurrence measures for cognitive tests to the value of the recurrence measure determined at rest. Thus, the resultant formula for calculation of normalized recurrence measures takes the form

$$RNRR^k = RR^{ek} - \frac{RR^{r1} + RR^{r2}}{2}. \quad (4)$$

Measures  $RNRR^k$  are plotted in Fig. 2 for all 19 EEG channels (calculated separately for each channel) and three groups of test subjects: (1) those fitted with braces; (2) those with aligners fitted over four teeth; and (3) those with aligners fitted over three teeth. Groups are marked with different colors and positioned differently. Figure 2, a corresponds to the first experiment (prior to correction); Fig. 2, b, to the second experiment (immediately after correction); Fig. 2, c, to the third experiment (two weeks after orthodontic treatment).

Patients were recruited from volunteers without neurological disorders and signs of cognitive decline. The exclusion criteria were as follows: ages under 18 and above 25 years; a HADS score  $\geq 10$ ; a body mass index  $\geq 25$ ; chronic pain experienced for more than six months; serious neurological and mental disorders in past medical history. Owing to the scarcity of patients who underwent orthodontic correction, groups 1 and 2 included three patients each (with a mean age of 20.7 and 21.1 years, respectively), and only two patients were in group 3 (the mean age was 20.3). In total, three women and five men participated in the study.

It can be seen from Fig. 2 that the recurrence measures in tests are, on average, lower than those in the state of rest.



**Figure 2.** Characteristics of distribution of recurrence measures of patients in the first (*a*), the second (*b*), and the third (*c*) experiments in different EEG channels and groups of patients. The data for the first (braces), the second (aligners over four teeth), and the third (aligners over three teeth) groups are represented in orange on the left, in green in the middle, and in blue on the right, respectively. A color version of the figure is provided in the online version of the paper.

The differences are especially significant in temporal lobes (channels T3–T6). Almost no differences between groups are observed in the first experiment with cognitive testing performed prior to correction. The following trend becomes apparent immediately after correction (Fig. 2, *b*): patients with aligners demonstrate a more profound recurrence measure reduction (relative to the state of rest) than patients with braces.

Two weeks later, the recurrence measure for cognitive tests in the second group of patients (with aligners fitted over four teeth) is the one closest to the state of rest. Recurrence measures of patients with aligners over three teeth and braces behave in a similar fashion in this case.

Thus, appreciable differences between groups of patients were revealed as a result of analysis of recurrence measures for EEG records made in the process of cognitive testing after orthodontic correction. The obtained results are correlated to some extent with those obtained in [14] with the use of much more complex methods (including the analysis of individual frequency ranges by wavelet transform). It was demonstrated in the present study that the most profound differences between patients with aligners over three teeth and braces are manifested immediately

after orthodontic correction, while the difference between patients with aligners over four teeth and braces becomes more pronounced two weeks after treatment. Assessments of painful sensations and stress (including the level of stress-induced bruxism) are planned to be used in future research for the purpose of estimating more accurately the effect of correction on cognitive functions. This analysis should help evaluate the level of stress experienced by a patient long after orthodontic treatment and, if needed, alter the therapy regimen.

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### Compliance with ethical standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All clinical

data and the clinical study design were approved by the Ethics Committee of the Saratov State University. All test subjects participated in the experiment voluntarily without compensation, signed the form of informed consent for participation in a clinical study, were given all the necessary explanations regarding the study, and gave their consent to publication of the study results. The obtained experimental data were processed with account for confidentiality and anonymity of participants.

### Conflict of interest

The authors declare that they have no conflict of interest.

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