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## Original Research Article

# Changes of electrophysiological parameters and neuropsychological characteristics in children with psychic development disorders after transcranial direct current stimulation (tDCS)

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## ABSTRACT

**Introduction:** Recently, school maladjustment that is associated with the cognitive decline in children with minor central nervous system disorders has become one of the topical issues.

**Aim:** The aim of this research was a retrospective analysis of changes concerning neurophysiological and neuropsychological parameters in children with psychic development disorders after treatment employing the transcranial direct current stimulation (tDCS) technique.

**Materials and methods:** Study data of 128 children with learning disorders and 48 children with mild mental retardation, aged 8–12 years old, who had undergone a course of tDCS, were analyzed. The data of neuropsychological testing and electroencephalography (EEG) of 22 healthy children and 42 children with psychic development disorders who had undergone conventional treatment, aged 8–12 years old, were used as a control. For tDCS procedures 60–120  $\mu$ A direct current was used, the stimulating electrodes area ranged from 2.5 cm<sup>2</sup> to 6.25 cm<sup>2</sup>. Treatment session duration (ranging from 25 min to 45 min), as well as stimulating electrodes localization onto the scalp and the time of the procedure, depended on clinical goals, age, and the severity of disorders. The entire treatment course duration lasted 4–5 weeks: 5–9 procedures with 2–3 day intervals.

**Results:** A neuropsychological study revealed statistically significant improvement of higher mental functions in patients undergoing tDCS compared to control groups. Verbal functions improvement was observed in 80.0% of children with such disorders. In patients with dysgraphia, after tDCS the rate of mistakes in writing reduced 3-fold, the process of writing quickened. The ability to fulfill tasks requiring visual spatial analysis and synthesis also considerably improved. After the course of tDCS no cases of negative changes of EEG parameters were noted. On the contrary, the improvement of EEG parameters, showing their approaching the age norms, was observed.

**Discussion:** The study results indicate that tDCS enables one to not only change directionally the functional status of brain areas lying under electrodes, but also to influence actively the

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functional status of deep regulatory brain systems through the changing of modulatory cortical areas status.

**Conclusions:** Having practically no adverse effects, tDCS appears to be an effective correction technique with respect to higher psychic disorders for children with psychic development disorders.

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## 1. Introduction

In recent decades, school maladjustment that is associated with the cognitive decline in children with mild central nervous system (CNS) disorders as compared with the age norms has become one of the topical issues.<sup>9</sup> It is caused not only by the increase in the number of patients with this pathology, but also by the lack of effective techniques of medical rehabilitation.

This necessitates the development and practical application of new techniques that would enable one to realize the high potential of a child's brain flexibility. Transcranial direct current stimulation (tDCS), which has been widely used in recent decades in neurophysiological studies for a direct changing of CNS structures excitability, is one of such techniques.<sup>15,17</sup> In Russia, this technique is termed "transcranial micropolarization."<sup>11</sup> The fundamental physiological bases for this technique, including safety and general principles for the clinical use issues, were developed in the 1970–1980s and presented in the publications of the Research Institute of Experimental Medicine of the Russian Academy of Medical Science (RIEM RAMS).<sup>16</sup> On the basis of these data, we have employed this technique in clinical practice since 1988. Nowadays, tDCS is our routine technique used in various neurological and psychoneurological cases.<sup>2,10,11</sup>

## 2. Aim

The aim of this research is a retrospective analysis of neurophysiological (electroencephalographical – EEG) data and neuropsychological changes in the course of treatment sessions of tDCS at different positions of stimulating electrodes onto the scalp.

## 3. Materials and methods

During the period of 1995–2009 at the Municipal Rehabilitation Center for Children with Psychoneurological Disorders more than 1300 patients, aged 9 months to 17 years old, underwent tDCS treatment. The results concerning 176 patients, who underwent tDCS, aged 8–12 years old, were selected for this analysis: 128 children (77 boys and 51 girls) with learning disorders (F81.3 by ICD-10) and 48 children (26 girls and 22 boys) with mild mental retardation (F70 by ICD-10). Neuropsychological testing results and the EEG data of 22 healthy children (13 boys and 9 girls), aged 8–11 years old, and randomly selected results of 42 patients (24 boys and 18 girls), aged 8–12 years old, with psychic development disorders who had undergone the conventional treatment (drug therapy, sessions with psychologists, logopedists, and ergotherapists) served as a control.

Patients with psychic development disorders were divided into 2 groups (Exp. 1 and Exp. 2) according to the Markovskaya classification.<sup>8</sup> Group Exp. 1 (60 patients) included children with predominating signs of brain structures morphofunctional immaturity with no evident clinical signs of neurological abnormalities. Group Exp. 2 (68 patients) included children with symptoms of organic disorders of cerebral structures that are exhibited as concomitant neurological disorders (soft neurological signs, general and oral dyspraxia, mild pyramidal and extrapyramidal insufficiency, etc.). The third experimental group – Exp. 3 (48 patients) included children with mental retardation. Children from the control group with psychic development disorders were also divided into subgroups: Cont. 1 (19 patients), Cont. 2 (13 patients), and Cont. 3 (10 patients), respectively.

Children in groups Exp. 1, Exp. 2, and Exp. 3 along with conventional treatment similar to that provided in control groups (except for drug therapy) underwent sessions of tDCS according to the techniques described in the literature.<sup>11</sup> A 60–120  $\mu$ A direct current was used, which enabled (taking into account the electrodes areas of 2.50–6.25  $\text{cm}^2$ ) one not to exceed the current density that is permissible for standard electrotherapeutical procedures of brain galvanization.<sup>18</sup> The equipment for medical electrophoresis Elfor-Prof (Nevoton, Russia) was used. The polarization session duration depended on clinical goals, age, and disorder severity level and ranged from 25 min to 45 min. A general course duration lasted 4–5 weeks: 5–9 procedures with 2–3 day intervals.

Three main electrode positions were used. The 1st position (a bipolar variant of tDCS, anode and cathode similar in size – 6.25  $\text{cm}^2$ ): the anode was positioned on the projection of the frontal cortex pole at the area Fp2 according to the international 10–20 system for EEG,<sup>1</sup> and the cathode was positioned on the ipsilateral mastoid region. The electrodes localization onto the subdominant hemisphere (for speech) in a bipolar position was used for all patients (the first 2 sessions). To define the dominant speech function lateralization, the dichotic listening was preliminary conducted.<sup>3</sup> A mild inhibitory influence on the subdominant hemisphere (tDCS during 35–40 min) enabled an activation reciprocally of the dominant hemisphere (for speech) by reducing the predominant hemisphere tonic inhibitory influence.<sup>14</sup> From the 3rd session in groups Exp. 2 and Exp. 3 the 2nd bipolar localization was used: the anode on the frontal region media-lateral surface, the cathode on the ipsilateral mastoid region. This localization was used for the alternate stimulation of subdominant (firstly) and dominant hemisphere structures (18–20 min for each hemisphere). This was dictated by the presence of paroxysms' signs in patients' baseline EEG parameters. Such a localization of the electrodes enabled an activation of the brain antiepileptic system structures, primarily the amygdale.<sup>16</sup>

The 3rd electrodes position (pseudo-monopolar stimulation): the anode (2.50 cm<sup>2</sup>) on the mid-frontal position 1 cm below Fpz according to the international 10–20 system, the cathode (6.25 cm<sup>2</sup>) on the ipsilateral mastoid region. At this localization, direct stimulation affected mesencephalic reticular formation and dorsal hypothalamus structures<sup>11,16</sup> representing part of the activating nonspecific brain system. This localization was used to affect the subdominant hemisphere structures in group Exp. 1.

In some cases short activating pseudo-monopolar stimulations (12–18 min, current strength of 100–120  $\mu$ A) were applied: the anode (2.50 cm<sup>2</sup>) was placed on the projection of cortical areas, the disorder of which had been revealed during a preliminary neuropsychological study (Broca area, Wernicke area, parietal association complex, etc.), the cathode (6.25 cm<sup>2</sup>) on the ipsilateral mastoid region. The attempts to place the cathode on the ipsilateral forearm or the ipsilateral cheek were clinically much less effective.<sup>11</sup>

All children in experimental groups before and after tDCS treatment and in control groups before and after the standard treatment course underwent complex clinical neurological, experimental psychological, and electrophysiological (EEG) examinations.

Experimental psychological examination included neuropsychological examination<sup>13</sup> supported with attention, operating memory, cogitation, and executive functions testing. For the evaluation of the majority of task results the 5-point quantitative/qualitative scale was employed.<sup>12</sup>

The EEG was registered in a quite wake state from 8 cortical areas according to the international 10–20 system: F3, F4 (frontal), T3, T4 (temporal), P3, P4 (parietal), O1, O2 (occipital) with an indifferent electrode on the ipsilateral ear using electroencephalograph Orion (Hungary) with the time constant 0.3 s, 30 Hz filters, analyzed epoch length 120 s, digitalization rate 250 Hz. The EEG power spectra and frequency spectra were analyzed. The statistical significance of EEG and neuropsychological parameters changes in experimental groups before and after the tDCS course and between the experimental and control groups were evaluated using the Mann-Whitney and Wilcoxon non-parametric tests.

#### 4. Results

The neuropsychological examination before the tDCS demonstrated a lack of active attention and reduced concentration

reaction in comparison with the group of healthy children of the same age in 60.0% of patients in both experimental and control groups. The most evident disorders were observed in groups Exp. 2, Cont. 2, Exp. 3, and Cont. 3. The short verbal memory was below the age norm in 65.0% of patients. Different severity levels of verbal function disorder were revealed in 44.0% of patients. The ability to solve problems constructively was reduced in 75.0% of patients.

Different severity levels of dysgraphia were revealed in 18.0% of children in Exp. 1 and in 16.0% in group Cont. 1, in 50.0% in group Exp. 2, in 54.0% in group Cont. 2, and in 100.0% of children in groups Exp. 3 and Cont. 3. Dyslexia was revealed in 4% of children in group Exp. 2, in 5.0% in group Cont. 2, in 50.0% in group Exp. 3, and in 46.0% in group Cont. 2. The events of dyscalculia were noted in 3% of children in group Exp. 1, in 5.0% in group Cont. 1, in 19.0% in group Exp. 2, and in 23.0% in group Cont. 2. Moreover, 48.0% of children in group Exp. 3 and 50.0% in group Cont. 3 were not able to perform simple denumerable operations.

The summarized results of the neuropsychological examination in the form of average values for each group are presented in Table 1.

In groups Exp. 1 and Cont. 1, higher psychic functions (HPF) deficiency was generally associated with modal-nonspecific factors and was evident mostly in disorders of neurodynamic characteristics of the psychic processes. In groups Exp. 2 and Cont. 2, modal-specific disorders of HPF as well as executive functions disorders, which are dependent on the prefrontal areas of the frontal cortex, were more often revealed. In groups Exp. 3 and Cont. 3, the degree of intensity and the incidence of HPF disorders were maximal. Statistically significant differences between experimental and respective control groups were not depicted ( $p > 0.05$ ), which demonstrated the uniformity of these groups.

Visual EEG analysis revealed evident deviations of brain bioelectrical activity (BA) as compared with the age norm. In all groups, the EEG parameters disorganization, no or poor frequency and amplitude modulation of rhythms, the excess of slow waves, the increased amplitude, pathological inter-hemispheric asymmetry, generalized and focal paroxysmal activity were noted. The absence of differences between the areas (more often in groups Exp. 2 and Cont. 2 as well as Exp. 3 and Cont. 3) or a decrease of differences (more often in groups Exp. 1 and Cont. 1), deformation, sharpness or duality of  $\alpha$ -waves peaks were observed. EEG activation periods were short and extremely low-grade. In spite of the polymorphous

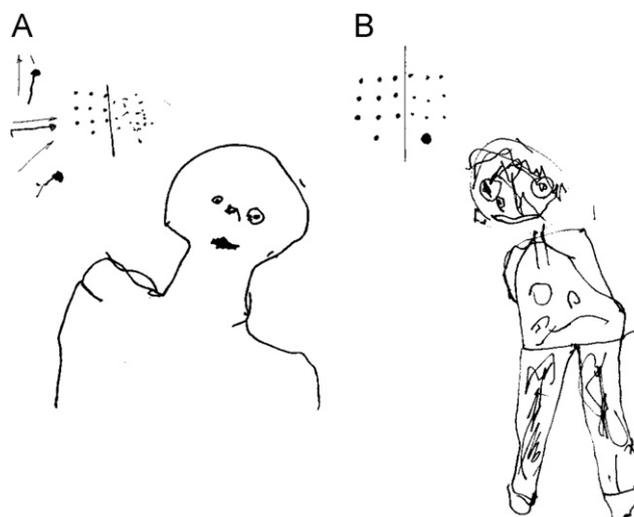
**Table 1 – Average scores ( $M \pm \sigma$ ) of performed tests of neuropsychological examination in patients of experimental groups and control groups before the treatment.**

Coefficient	Experimental groups			Control groups		
	Exp. 1	Exp. 2	Exp. 3	Cont. 1	Cont. 2	Cont. 3
$K_1$	4.6 $\pm$ 0.22	4.0 $\pm$ 0.60	2.5 $\pm$ 0.4	4.5 $\pm$ 0.35	3.9 $\pm$ 0.41	2.6 $\pm$ 0.28
$K_2$	4.4 $\pm$ 0.34	3.6 $\pm$ 0.41	2.4 $\pm$ 0.4	4.4 $\pm$ 0.24	3.8 $\pm$ 0.33	2.4 $\pm$ 0.42
$K_3$	4.0 $\pm$ 0.51	3.1 $\pm$ 0.40	2.4 $\pm$ 0.38	4.1 $\pm$ 0.44	3.3 $\pm$ 0.40	2.5 $\pm$ 0.37
$K_{sum}$	4.3 $\pm$ 0.36	3.6 $\pm$ 0.21	2.4 $\pm$ 0.35	4.3 $\pm$ 0.30	3.7 $\pm$ 0.25	2.5 $\pm$ 0.37

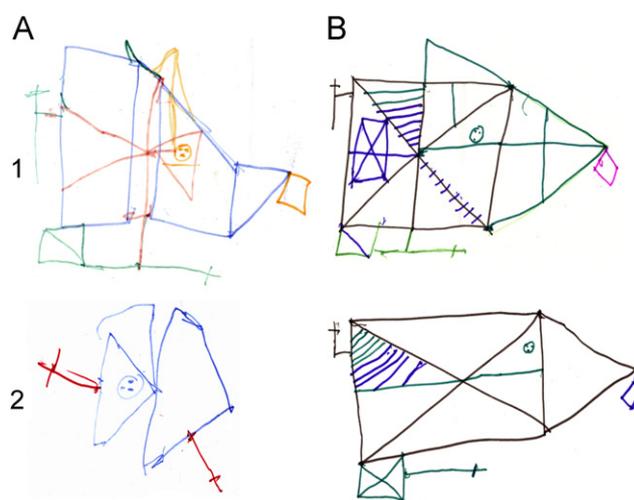
Comments:  $K_1$  – intelligence “preconditions” – average assessment of kinesthetic basis of movement, visual spatial organization of movement, visual gnosis, stereognosis, auditory-motor coordination;  $K_2$  – average assessment of verbal functions;  $K_3$  – average assessment of nonverbal functions;  $K_{sum}$  – total mean score of higher psychic functions.

character of BA, particular differences between the EEG parameters of patients in study groups were observed. For example, in groups Exp. 1 and Cont. 1 the character of BA changes generally indicated the brain structures immaturity, decreased effects of ascending activating system (mesencephalic reticular formation and dorsal hypothalamus), and signs of mild diencephalic structures dysfunctions, which is reflected in mismatching the EEG parameters to age norms (in 80.0% of cases), low grade activation changes of the EEG parameters, the presence of  $\alpha$ -activity (with the index of more than 50.0%) in frontal areas, and the occurrence of  $\theta$ -waves bursts and paroxysms. At the same time, in some patients the signs of mesencephalic systems hyperactivation, such as low amplitude slow activity interleaved with high frequency components, often with spindle components, were noted. In groups Exp. 2 and Cont. 2, along with more evident aforementioned disorders, signs of local disorders (mainly in temporal and parietotemporal areas) were detected as well as more evident involvement of diencephalic structures in the pathological process (the presence of  $\alpha$ -rhythm bursts, mainly in frontal and central areas). In groups Exp. 3 and Cont. 3, pathological changes were observed more often and were more evident. Paroxysmal activity, the presence of complex-like waves (occasional combinations of sharp and slow waves), sharp waves, and  $\delta$ -waves were observed in 28.0% of the analyzed EEG results. A large number of diffuse high-amplitude  $\theta$ - and  $\delta$ -waves in frontal and central areas were notable; they were more evident in a dominant (for speech) hemisphere. All these facts indicated a larger involvement of cortex and brainstem structures in the pathological process in comparison with patients in groups Exp. 1 and Exp. 2. None of the patients in treatment groups had a history of seizures. Visual BA analysis did not reveal specific changes that would be typical of any particular study group; although, on the whole, severe BA disorders were observed among patients in groups Exp. 3 and Cont. 3, and less evident disorders were noted in groups Exp. 1 and Cont. 1; the EEG parameters of patients in groups Exp. 2 and Cont. 2 were intermediate.

The next experimental psychological examination conducted after the tDCS course demonstrated a significant improvement in the attention function almost in all patients in those experimental groups in which it had been decreased. Children were able to memorize more frequently and quantitatively both verbal and nonverbal information. In 80.0% of children with an insufficient verbal function its improvement was observed. Quantitative assessment of treatment efficacy in children with dysgraphia (calculation of mistakes in writing) demonstrated an evident reduction of mistakes quantity after tDCS from 2- to 6-fold in different children (3-fold on average). All children began to write with less effort; the hand became tired less than previously noted, the process of writing quickened. Evident changes in the children's ability to fulfill tasks requiring visual spatial analysis and synthesis were noted. Fig. 1 demonstrates test drawings of the "Goodenough Draw-A-Man Test" and points copying<sup>12</sup> of patient G., 6 years old, from group Exp. 2 before and after treatment. After the tDCS course, patient G. managed to copy points correctly, the drawing of a man became more complex and accurate.



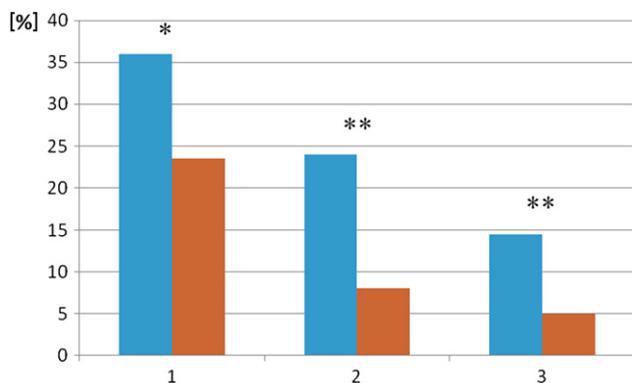
**Fig. 1 – Drawing-tests: the “Goodenough Draw-A-Man Test” and points copying performed by patient G., 6 years old, from group Exp. 2 before (A) and after (B) the tDCS course.**



**Fig. 2 – The Rey-Osterreith complex figure test performed by patient K., 12 years old, from group Exp. 2 before (A) and after (B) the tDCS course: 1 – copying of a figure; 2 – reproduction of a figure from memory.**

The results of copying and the Rey-Osterreith complex figure reproduction<sup>7</sup> of patient K., 12 years old, from group Exp. 2, that was done 2 weeks before treatment and 1 month after the end of tDCS procedures are presented in Fig. 2. An evident visual spatial function improvement can be seen as well as improvement with regards to the ability of planning, control, and regulation of psychic activity, which are dependent on prefrontal cortex functioning.

Fig. 3 demonstrates the average values of neuropsychological parameters approaching the age norms in patients in experimental groups (after the tDCS course) and control groups (after a standard rehabilitation course). As can be seen, the average assessment  $K_{sum}$  in all experimental groups approached the norms significantly more than in the control groups.



**Fig. 3** – The average values of neuropsychological parameters approaching the age norms. The difference between parameters of the age norm and the initial recorded parameters was taken as 100.0%. Blue bars – patients undergoing tDCS, red bars – patients of control groups. Comments: 1 – Exp. 1 and Cont. 1 patients; 2 – Exp. 2 and Cont. 2 patients; 3 – Exp. 3 and Cont. 3 patients; \* – statistically significant differences at the level of  $p < 0.05$ ; \*\* – statistically significant differences at the level of  $p < 0.01$ .

Neuropsychological examinations conducted for some patients (68 patients) 6–8 months following the tDCS course termination demonstrated that the achieved effects not only remained following this period of time, but also increased even in those patients with mental retardation. As early as 2 weeks after the tDCS course, the EEG results of patients in all experimental groups demonstrated a minor (9–11%) increase in the quantity of  $\alpha$ -waves as well as a significant increase in the  $\alpha$ -rhythm control frequency at 1.0–1.5 Hz on average, an improvement in the  $\alpha$ -rhythm between-area distribution, a decrease of paroxysmal activity and the quantity of sharp waves in response to the functional load. At the same time, a decrease of the  $\delta$ - and  $\theta$ -range indexes was observed. However, in nearly all leads these changes were insignificant and registered as tendencies with the exception of the right frontal and right temporal areas (which had been primarily exposed to tDCS) in patients in groups Exp. 1 and Exp. 2, where a significant ( $p < 0.05$ ) decrease in the quantity of  $\beta$ -waves and an increase in the quantity of  $\delta$ -waves were observed. Similar changes were observed in patients with dysgraphia, dyslexia, and dyscalculia in projections of areas exposed to the direct anode tDCS (the left angular gyrus projection and Wernicke and Broka areas). In control groups no significant changes in the EEG parameters were noted.

## 5. Discussion

Clinical psychological and electrophysiological changes indicate the effect of tDCS on the entire brain regulatory system, which results in the comparative normalization of the general neurodynamics of the brain, as well as in the local functioning of particular regulatory systems.

General clinical physiological changes observed in nearly all patients involve EEG parameters improvements that characterize CNS morphofunctional maturity (matching the age norm, an increase in high-frequency rhythms and a decrease in slow components, the  $\alpha$ -rhythm between-area distribution improvement, etc.). General nonspecific changes include such psychic functional changes as the improvement of attention, memory, concentration reaction, working capacity increase, etc. These changes were observed to a greater or lesser extent in nearly all patients that had undergone tDCS.

Specific changes include improvement in reading and writing abilities exhibited by patients with various forms of dysgraphia and dyslexia, visual spatial function in patients with lower parameters of nonverbal intelligence.

The most probable mechanism for the achievement of cognitive functions modal-nonspecific improvements that were observed in nearly all patients after tDCS is a nonspecific stem systems activation leading to the brain neurodynamics normalization and the intensification of morphofunctional development of association systems. A similar phenomenon is observed in rostral reticular formation stimulation in stereotactic operations.<sup>14</sup> The possibility to affect directly the brain nonspecific activation system structures by means of mild direct current polarization, which modulates frontal and temporal cortical areas, was experimentally demonstrated at RIEM RAMS<sup>16</sup> and was confirmed by the present research.

A decrease in the pathological EEG activity in the course of tDCS may be explained by the brain antiepileptic system activation (mostly the lateral amigdala) as well as the acceleration of the CNS structures morphofunctional development. The most probable mechanism for specific clinical effects of tDCS appears to be the changes that occur in the polarization area under the electrode (mostly under the anode) and in the area of the maximal polarization focus (in the middle between the electrodes). Thus, it appears interesting that the slow components of EEG recordings become significantly more evident exactly in these areas. In the overwhelming majority of clinical studies, a local increase in the quantity of  $\delta$ -waves is considered as an adverse symptom associated with the cortical inhibition aggravation that leads to a decrease in functions. At the same time, the cognitive improvement that was observed in the present study is associated with functional improvement of exactly these brain areas. It may be assumed that in this case our results, that had been considered by Bekhtereva,<sup>1</sup> indicate not only the lack of an obvious association of slow waves with the inhibition process, but also their positive role in the processes of compensation and reorganization in the CNS. If this is the case, the increase in the regional slow-wave activity that was observed can be considered to be a reflection of the functional reorganization that occurs in the areas exposed directly to tDCS. In electron microscopic studies of tDCS, in the areas precisely under the electrodes, maximal ultrastructural changes of neurons and their synaptic apparatus are revealed.<sup>16</sup> The functional changes of cortical areas in the course of tDCS should not be considered as a simple increase or decrease in cortical elements excitability. A prolonged duration of the obtained effects and their progressive positive dynamics indicate that some long-term qualitative changes occur in the polarization area.

The potential concerning the integration of small groups of neurons into integral functional microsystems under the influence of the local polarization of cortex was shown in several research studies.<sup>1,5,6</sup> Such neuron systems play an important role not only in simple effector reactions, but also in HPF.<sup>5</sup> Specific clinical effects achieved in the course of tDCS may be explained not only by a reorganization of functionally ineffective neuronal complexes in polarized areas, but also by their active involvement into integral brain activity. The potential of the microcirculation improvement and the intensification of metabolism in the brain tissue cannot be disregarded, which is confirmed in studies concerning tDCS in animals.<sup>16</sup> Neurophysiological mechanisms of tDCS effects also require a special consideration. From the experimental-physiological point of view, polarization conducted over pia mater and dura mater of the brain and over a bone is inefficient since there are many ways of current drain (spongy bone, liquid layers between meninges, etc.) that make the results of stimulation not local enough and thus difficult to predict. In such a case, an evident current strength extension is necessary for the achievement of physiological effects. As has been shown,<sup>4,18</sup> the current strength that is needed for the depolarization of nervous cells membranes resulting in the action potential at the extracranial polarization exceeds in magnitude that permissible for electrotherapeutic procedures, such as galvanization, and thus exceeds 100-fold that used in our study.

Thus, using such parameters of direct current as in this study, it becomes impossible to consider the idea of a direct depolarization of cortical cells membranes. The most probable mechanism for achieving the local polarization effects with extracranial direct current stimulation may not be the direct influence of the current on the brain cells but rather the modulation of the electrostatic field influence. The application points of these fields are the excitable neurons themselves and their electrotonic contacts.

## 6. Conclusions

Our findings enable us to conclude that tDCS is an advanced technique to enable HPF disorders correction in children with psychic development disorders. Having practically no adverse effects, tDCS enables one to change directly a functional state of different brain structures and to influence actively the processes of self-organization and self-reorganization of brain regulatory systems.

## Conflict of interest

None declared.

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