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Age-Related Changes in EEG Formation during Transcranial Direct Current Stimulation

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Abstract—The EEG power spectra in the main bands (4 to 20 Hz) were compared during transcranial direct current stimulation (tDCS) treatment in children with mental development disorders of perinatal origin. In resting state with the eyes closed, a shift in the average frequency of α activity in the parieto-occipital area (from 9 to 10 Hz) and an increase in the spectral power stronger in the right hemisphere were observed. With the eyes open and closed, a decrease in the β range power spectrum in the right posterior temporal cortex was observed in children undergoing tDCS treatment. The power spectra of θ activity with a frequency of 4–5 Hz in the left posterior-temporal area with the eyes open showed negative correlation with age.

Keywords: electroencephalogram, mental disorders, perinatal central nervous system disorders, transcranial direct current stimulation (tDCS)

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It is known that children with mental development disorders frequently exhibit, along with paroxysmal EEG activity, signs of immaturity of age-related biorhythm patterns, such as insufficiently pronounced parieto-occipital focus of α activity or elevated share of slow θ range waves in comparison to age norms [1–10].

In our previous study that involved preschool children with a history of perinatal encephalopathy, it was shown that the share of immature EEG patterns in normally developing children did not exceed 15%, whereas in those with cognitive and speech delay, it was as high as 55.3% [11]. It was also found that, in children with mental development disorders who exhibited positive developmental dynamics with conventional drug therapy, EEG showed signs of immaturity in 43.6% of cases.

In contrast, in the group that did not show positive response to therapy, this number increased 61.0% (the difference was significant at $p < 0.001$). It was in this group that we investigated EEG patterns during treatment using transcranial direct current stimulation (tDCS) course aimed to stimulated speech and mental development. In our previous study in children with mental development disorders, we identified hypothetical sources of low-frequency activity in the frontotemporal areas of the brain cortex and observed an increase in the power of slow components that correlated with severity of developmental delay [12]. A longitudinal study of power spectra of the main EEG ranges performed in the same group of children at different stages of correction therapy using tDCS detected a significant increase in the level of α activity in the parieto-occipital regions of the brain cortex, as well as a significant decrease of the slow-wave activity in the frontotemporal region of the left hemisphere [13]. These changes were detected in mental development disorders children with different initial EEG types (e.g., asynchronous, hypersynchronous, without regional differences).

The goal of the present study was to identify the patterns of age-related dynamics of bioelectrical brain activity in children with mental and speech development disorders of perinatal origin in the course of tDCS treatment.

METHODS

Clinical EEG studies were performed in 124 children aged three to eight years with a history of perinatal encephalopathy; EEG was recorded in waking subjects with the eyes open and closed. EEG is a standard examination required for admission for a tDCS course to exclude epileptiform activity. The control group included 69 children (32 girls) with normal development; mean age, 5.9 years (SD = 1.6). The second group included 27 children (4 girls) with mental and speech development disorders who were undergoing conventional treatment (pharmacological therapy with cogitum, cortexin, gliatilin, and other drugs, logotherapy, and other); their mean age was 5.6 years (SD = 1.1). The third group included 28 children with mental development disorders (7 girls; mean age was 6.1, $SD = 1.4$) who received treatment using tDCS. Based on the previously obtained data [13], group 3 was divided into two subgroups according to the number of tDCS courses completed: subgroup 3a had one to three courses, and subgroup 3b had more than three courses. For the purposes of comparison, the groups were age-matched using the Mann–Whitney U test.

EEG was recorded at rest during 2–4 min. Ag/AgCl electrodes were positioned according to the 10–20 international system. EEG was recorded from 19 electrodes using a computer-based Mitsar electroencephalograph (Russia). All electrode impedances were kept below 5 kΩ. Unipolar recording was performed relative to the right and left Ag/AgCl ear electrodes. The low- and high-frequency band pass parameters were 0.5 and 45 Hz, respectively. Correction of eye movement artifacts was performed by filtering the independent components corresponding to these movements with a focus on the frontal leads Fp_1 and Fp_2 [14]. The method of independent components was applied because of small duration of artifact-free EEG [15]. EEG fragments that contained artifacts of rapid oscillations with a frequency of 20 to 35 Hz and amplitudes exceeding 20 μV, slow waves with a frequency of 0 to 1 Hz exceeding 50 μV, as well as a potential jumps of over 120 μV were excluded from the analysis. The study was performed using the common average reference (Av) monopolar montage.

Comparative analysis of the power spectra was performed in the main EEG ranges: θ (4–8 Hz), α (8–13 Hz), and β (13–20 Hz). The spectra were calculated using the following parameters: standard epoch length, 2 s; epoch overlap, 50%; Hanning time window. For comparison, the power spectra of a given EEG range were normalized to the total power spectrum in the range of 1 to 20 Hz and averaged over each group of children.

Correlation analysis of age-rated dynamics was performed using the Pearson correlation coefficient; to obtain normal distributions, logarithms of the mean values of the power spectra were calculated.

tDCS was performed with a focus on the left hemisphere region near the cortical projections of speech centers and association areas according to the patented techniques [11, 16]. The projections of brain landmarks on the head surface were verified using the coordinates of the R.Krönlein topographic map [16]. tDCS was performed using a commercial apparatus for physiotherapy (ELFOR-prof; License no. FSR 2010/08893). Conductive rubber electrodes (area, ~3 cm^2) were placed on the patient's scalp over six to eight layers of flannel. The duration of exposure was 20 min, the current intensity was 40–120 μA (according to the patient's well-being), and the current density were 13 to 40 μA/cm^2, respectively. The cathode was placed at the mastoid bone or the occipital bone projection near the foramen of the same hemisphere as the anode. The anode position was selected based on the neuropsychological relationship between the impaired brain function (e.g., speech perception and production, gross and fine motor skills, or associative activity) and the corresponding target area related to the given function (Brodmann areas) [16]. The number of sessions per courses was previously determined empirically as patient's age ± 1 based on the patient's well-being, in the absence of consistent side effects. The pause between the tDCS courses was 6–12 months.

RESULTS

Comparative analysis of the power spectra of waking EEG revealed the following differences (Fig. 1).

With the eyes closed, the level of α activity at 8 and 10 Hz in the parieto-occipital focus was lower in conventionally treated children with mental development disorders (group 2) than in the control group (group 1), but this trend was not statistically significant (Fig. 1A).

In group 3a (one to three tDCS courses), the level of α activity at 8 Hz in the parietal cortex (Pz, P_4) was decreased in comparison to control, but this decrease was not significant ($p < 0.98$) (Fig. 1B, column a). An elevated share of α activity with a higher frequency (9 Hz) was also observed in the posterior regions, which was stronger on the right (Fig. 1B, column b), but these differences were also present as a trend and did not reach the significance threshold ($p < 0.27$).

Finally, in group 3b (more than three tDCS courses), the trend described above was significant at 10 Hz and was stronger in the right hemisphere ($p < 0.02$, Fig. 1C, column b). Low-frequency α activity (8 Hz subrange) also exhibited power changes, but they were not statistically significant (Fig. 1C, column a).

The power spectra of the β range exhibited significant differences depending on the number of tDCS courses (Fig. 2). They were observed in the right posterior-temporal cortex area (T_6), where the power of β activity was lower in the subgroup that underwent more tDCS courses, and were more pronounced with the eyes open than with the eyes closed (Fig. 2). In EEG with the eyes open, the power spectra of α and θ ranges had no significant differences between the groups 1, 2, and 3.

Correlation analysis detected differences in the low-frequency range of EEG recorded with the eyes open (scatter diagrams in Fig. 3). In particular, there was an inverse correlation between the θ range activity (4–5 Hz) in the left posterior temporal region (T_5) and the age of children with ~~MDD~~. In other words, the power of θ activity at these frequencies decreased with age in both groups of ~~MDD children~~ (treated with conventional therapy and tDCS). In the group receiving conventional therapy, these differences were

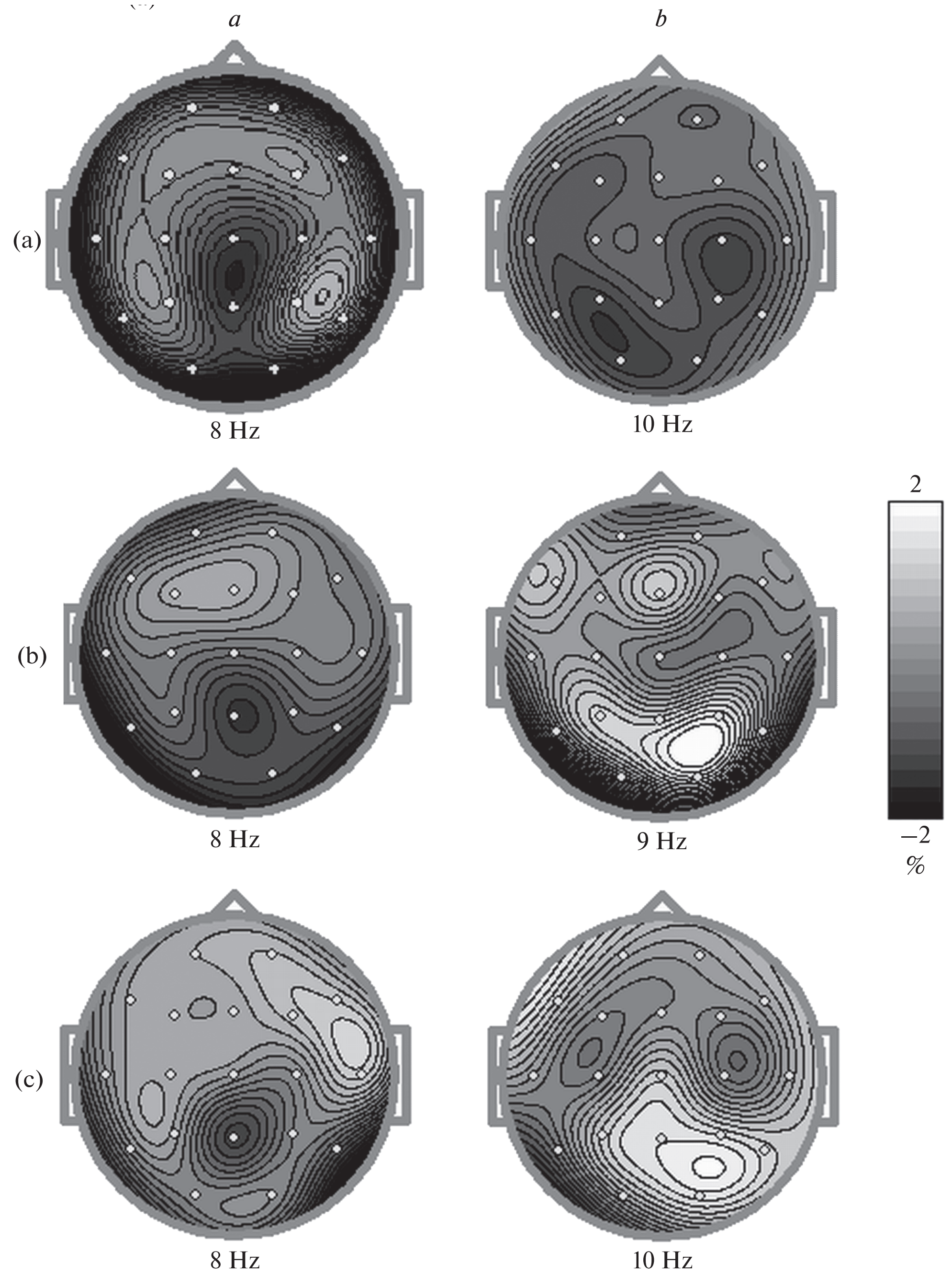

Fig. 1. Comparison of waking-state alpha-range power spectra in children with mental development disorders (eyes closed). (a) Difference between the spectra of group 2 (conventional therapy) and control group 1; (b) Difference between the spectra of subgroup 3a (one to three tDCS courses) and control group 1; C, significant difference between subgroup 3b (more than three tDCS courses) and the control group. Column *a*, topograms for the mean frequency of 8 Hz; column *b*, for the frequencies of 9 and 10 Hz. The values in the topograms are shown in relative units as percent of the total EEG spectrum in the range 1–20 Hz.

observed as trends that did not reach the significance threshold (Fig. 3A, group 2, $r = -0.31$, $p < 0.11$). At the same time, in the tDCS group, these differences in power were significant (Fig. 3B, group 3, $r = -0.57$, $p < 0.001$). This particularly important, because initially the mean power of the θ activity spectra in younger children of the tDCS group was nearly twofold higher (Fig. 3B, X axis) than in children with conventional therapy (Fig. 3A).

DISCUSSION

Electrophysiological characteristics exhibit broad variation due to individual features of children's devel-

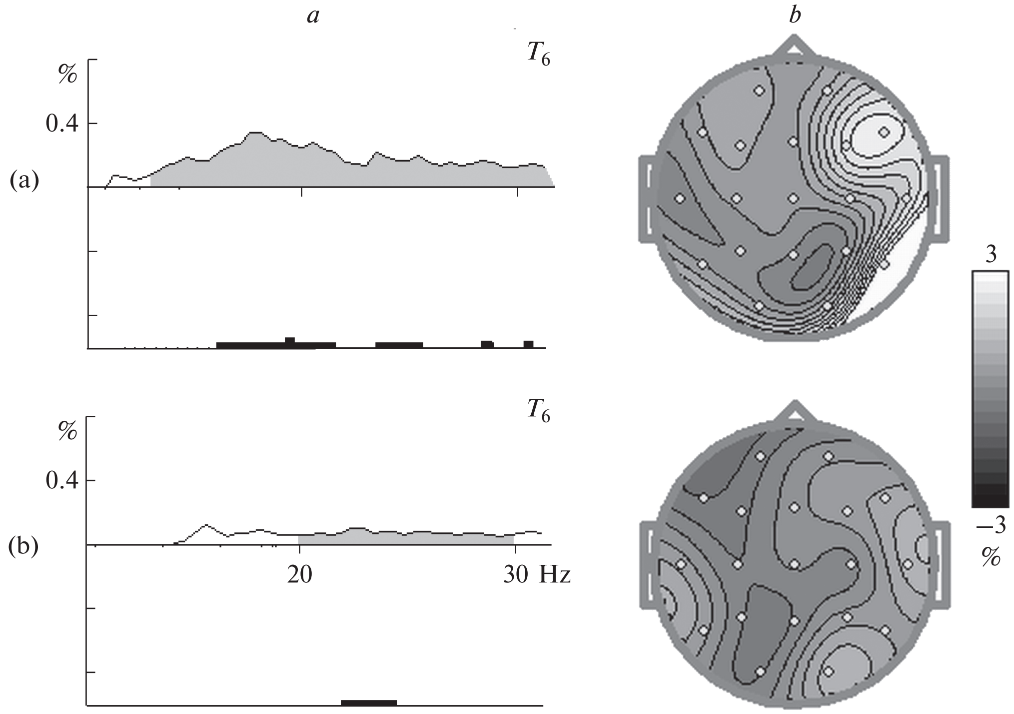

Fig. 2. Analysis of the β-range EEG power spectrum in the right posterior–temporal area (T_6 according to the 10–20 system) during tDCS treatment. (a) Waking state, eyes open; (b) eyes closed. *a*, *X* axis, frequency in hertz; *Y* axis, the difference between power spectra in groups 3a and 3b, relative units; the analyzed EEG ranges are filled with gray. Significant differences ($p < 0.05$) are shown in bold below the chart. *b*, topograms of the detected differences over all leads.

opment and the difference of EEG patterns (amplitude–time parameters and spatial rhythm organization). This concerns both single-time and repeated studies that involve children differing in age, severity of developmental delay, and at different stages of correction therapy. In our previous longitudinal study that analyzed waking-state EEG with the eyes closed in the same group of children in the course of correction treatment using tDCS, we observed a significant increase in the power spectrum of the main α rhythm in the age-specific parieto-occipital focus without pronounced lateralizaton, as well as a significant decrease in the slow-wave activity in the frontotemporal area of the left hemisphere [13].

In the present study, which was aimed at investigating the effects of tDCS course treatment, we identified a significant shift of the α range power spectrum to higher frequencies (9–10 Hz subrange), which was more pronounced in the right hemisphere, although 95% of tDCS sessions were performed in the left hemisphere. Previously, we described interhemispheric asymmetry of EEG of the children with mental development disorders without tDCS, in particular, it was a decrease in the power spectra of different EEG ranges in the left hemisphere. [11]. The data obtained are still insufficient to enable a definite conclusion as to whether delayed mental development involves abnormal interaction between hemispheres as a result of perinatal CNS damage, as well as predomination of forced left-handedness [17–26]. Another controversial issue is whether tDCS actually promotes interhemispheric equilibrium by enhancing the biological capacities of the damaged site, or rather the tDCS effects are of compensatory nature and stimulate the intact elements of the system to take on the functions of the damaged elements. Apparently, our data on the effect of physiological intervention on the interhemispheric asymmetry supports the notion that the relationship between the right and the left hemisphere is consistent with the part rather than the whole paradigm [17].

The processes of cortical rhythm acceleration involved not only the α range, but also slow-wave activity, which became less represented in the total EEG spectrum, such as in children with more pronounced delay who received tDCS treatment, in whom the initial power of slow waves was nearly twofold higher than in those patients who had a satisfactory response to conventional drug therapy.

We also analyzed the β-range activity, since our previous study performed in patients with autistic spectrum disorders using independent component analysis identified a localized focus of β activity in the right occipital area [27]. This study showed that tDCS treatment led to a significant decrease in the β wave power in the right posterior temporal area. Probably,

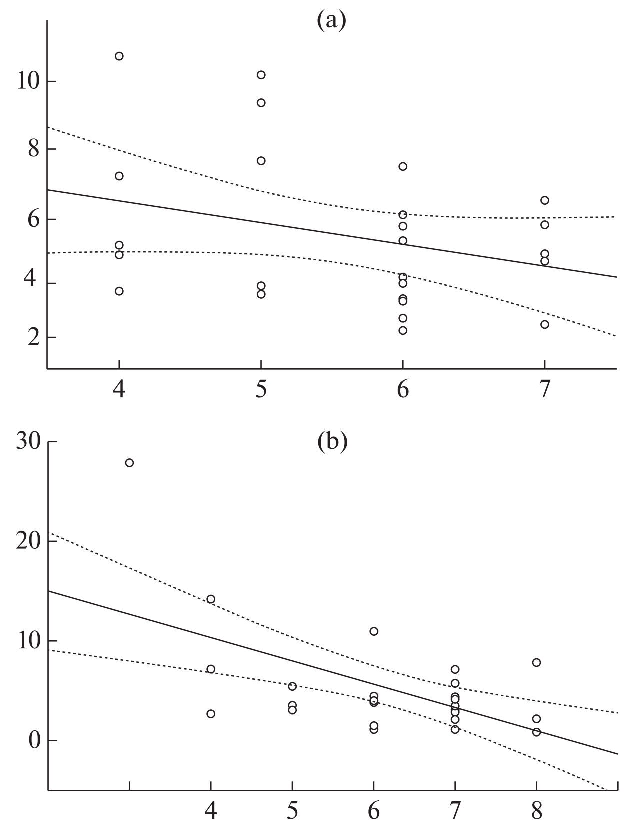

Fig. 3. Correlation analysis of θ-range EEG power spectra in the left posterior temporal area (T_5) in children with mental development disorders recorded in waking state (eyes open). (a) A scatter diagram for group 2 mental development disorders without tDCS treatment); (b) a scatter diagram for group 3 (mental development disorders with tDCS treatment). *X* axis, age (years); *Y* axis, mean values of the power spectrum of θ waves in the range 4–5 Hz (μV^2).

the involvement of posterior cortex areas is a non-accidental finding, since at least 50% of children in the tDCS group exhibited behavioral patterns described as autistic features of varying extent (such as avoidance of tactile and eye contact, indifference to relatives and other children, poor response to name, the lack of communicative speech, stereotypies, or limited food selection).

In our research, we have employed both the longitudinal design (repeated studies in the same group children) and the age cross-section approach (studies in different groups of children), which provides a more coherent view of the changes in the electrophysiological brain activity in children with impaired mental and speech development. Using group comparison to diminish the effects of individual bioelectrical activity features, we were able to distinguish general patterns of EEG rhythm dynamics during tDCS treatment, both in the frequency parameters and in the local accents of significant changes in power spectra. By accumulating EEG data during long-term monitoring of children undergoing tDCS treatment, we expect to complement the comprehensive pattern of positive changes in brain activity induced by targeted treatment in the case of developmental disorders.

CONCLUSIONS

To sum up, children with mental development disorders of perinatal origin undergoing tDCS treatment exhibited the following significant differences in the main waking EEG rhythms:

(1) With the eyes closed, the power spectrum of α activity in the 9–10 Hz range in the parietal-occipital regions was increased, more pronouncedly in the right hemisphere (after more than three tDCS courses).

(2) With the eyes open and closed, the power spectrum of β activity in the right posterior temporal area of the brain cortex was decreased.

(3) With the eyes open, the power spectrum of θ activity in the 4–5 Hz range in the left posterior temporal area decreased with age (negative correlation).

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COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interests. The authors declare that they have no open or potential conflicts of interests related to the publication of the present article.

Statement of compliance with standards of research involving humans as subjects. All procedures involving human participants were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments and were approved by the Committee on Bioethics of the *N.P.* Bechtereva Institute of the Human Brain. Informed consent was obtained from all individual participants involved in the study. All participants signed a written informed consent form after being informed about the potential risks and advantages, as well as about the design of the study.

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