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Brain Structural and Functional Characteristics in Children with Mental Disorders and the Possibilities of Transcranial Direct Current Stimulation

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Abstract—Analysis of the magnetic resonance imaging (MRI) data in children with mental disorders of perinatal origin showed that, in 70% of cases, pathological damage to the brain structures is absent, or only minimal residual changes are detected. At the same time, the EEG α-rhythm in the occipitoparietal areas was not regular in 77% of cases. The predominance of the signs of cerebral functional insufficiency allows efficacious use of the physiological methods of correction of mental disorders using transcranial direct current stimulation.

Keywords: perinatal CNS pathology, MRI, EEG, mental disorder, learning disorders, autism spectrum disorders, transcranial micropolarizations (TCMP, tDCS).

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The persistence of negative trends towards the growth of children with developmental higher mental functions (HMF) and speech disorders, considerable difficulties in learning and social integration make the studies of the cerebral mechanisms of formation of developmental deviations and the elaboration of effective methods for their correction especially important. At present, the use of weak direct current (transcranial micropolarizations (TCMP)) as a direct physiological exposure in various brain disorders has been substantiated well enough in the theoretical, experimental, and clinical aspects.

METHODS

Children aged 3 to 7 years with mental disorders that developed against the residual organic background due to perinatal CNS damage were examined (Table 1). Children with hereditary pathology were not included in the study.

The level of HMF and speech development was tested using the standardized methods [15]. When assessing the mental activity changes influenced by TCMP, we employed the principles of Luriya's theory about the main functional blocks of the brain [16]. The functions to be assessed were grouped as follows. Block I was the tone and wakefulness regulation block characterizing the general level of psychomotor activity of a child. In connection with the leading function of speech in the formation of child psyche, the speech processes were singled out as a separate block (II). Block III included the rest of the HMF: sensoriperceptive processes, the emotional–volitional sphere, memory, mental operations, etc. Block IV was used for evaluating the programming, control, and regulation of activity.

Johnkir's nonparametric *S*-test of trends [17] was chosen to estimate the significance of changes in a large number of parameters (groups of children, TCMP courses and sessions, four HMF and speech blocks assessed). It allowed us to identify a nonrandom increase in the values of the sign studied, in particular, an increase in the level of development of one or another mental process influenced by the course of TCMP in different groups of children.

In order to assess the level of development of children with autistic spectrum disorders (due to difficulties of the standard testing), the international ADOS questionnaire, which was completed by parents, and the Woodcock–Jonson independent behavior scale were used before TCMP courses (cited according to [18]). The significance of changes in mental development in the course of TCMP was assessed in this group using Wilcoxon's test.

The EEG recording was carried out with a Mitsar computer encephalograph. Silver chloride bridging electrodes were arranged according to the international 10–20 system; the recording was made in the following frequency band: the lower border, the time constant 0.1 s; the upper border, 50 Hz. The EEG electrode resistance did not exceed 5 kΩ. The recording was carried out in the monopolar mode in relation to the right and left aural silver chloride electrodes and bipolarly in a resting state for 2–4 min with the eyes

Table 1. Groups of examined children with different forms of developmental HMF and speech disorders

Groups of children	The number of the children examined	The number of TCMP sessions
1, speech disorders with normal HMF	38	185
2A, combined HMF and speech disorders without autistic symptoms	62	511
2B, combined HMF and speech disorders with autistic symptoms	42	295
2C, early infantile autism (EIA)	29	214
Total	171	1205

See text for the abbreviations in Tables 1–7.

Table 2. Structural characteristics of the brain of children with retardation of HMF and speech development

MRI findings	The number of children	
	the absolute number ($n = 105$)	%
Without pathology	40	38.1
Minimal residual changes, the signs of compensated hydrocephaly	34	32.4
Total	74	70.5
Changes in the brain (small cysts, atrophic foci, cerebellar hypoplasia, Dandy–Walker malformation, etc.)	31	29.5

open and closed. The Win EEG software was used for EEG processing. The presence/absence of the occipitoparietal α]-rhythm focus was assessed [9, 19].

The studies of the brain structures of children for medical indications were conducted using a Philips Achieva 3 T MRI scanner. When TCMP was carried out to pinpoint the projections of intracerebral reference points on the head surface, the coordinates of Krenlein craniocerebral topography scheme used in operative surgery were employed [20]. The proposed scheme allows the projection of the main cerebral hemispheric fissures and convolutions onto the skull surface. In order to ensure the required accuracy of exposure, the coordinates of the main labels fixed before MRI performance on the head skin surface in the region of the cortical projections of TCMP targets according to the 10–20 scheme, as well as those of the reference elements of the patient's ventricular system, were determined in pilot investigations. With the software for IBM-compatible computers (developed by Yu.Z. Polonskii), we converted the coordinate values of the boundaries of cortical fields and the labels corresponding to them to the system of stereotactic coordinates of Talairach's atlas (cited from [21]).

TCMP was performed using a serial device for physiotherapy (ELFOR-prof, registration certificate no. FSR 2010/08893 issued by the Ministry of Health and Social Development). The electrodes made of conductive rubber (an area of about 3 cm^2), which were arranged under the EEG helmet on a child's head skin through six to eight layers of the 30-mm flannel padding moistened with tap water, were used. The exposure time was 20 min; the intensity of exposure, 40–120μA; current density, 13 to 40 $\mu A/cm^3$, respectively. The number of sessions per course was determined by the child age ±1 scheme and varied in preschool children between 2 and 7 days (based on the well-being). The cathode was arranged on the mastoid process or in the projection of the occipital bone near the occipital foramen of the ipsilateral (relative to the anodal position) hemisphere. The anodal position was selected based on the principle of neuropsychological correspondence between disordered mental functions (impressive, expressive speech, coarse and fine motor skills, associative activity, etc.) and the target region (Brodmann's areas) connected with this function [16, 22].

RESULTS

The MRI data analysis showed that, in 70% of children with a delay in mental and speech development (retardation of mental development against the residual organic background, coarse delay in mental development due to organic CNS lesions, etc.), pathological changes in the cerebral structures either were not revealed or minimal residual changes (single small foci of lesions of the white matter of posthypoxic character, the signs of compensated hydrocephaly, etc., see Table 2) were observed. In one-third of children, MRI changes were represented by small cysts; aorigin or hypoplasia of the corpora callosum, cerebellum; Dandy–Walker malformation variants, etc.

Table 3. Provisional TCMP targets in preschool children with mental disorders in groups 1 and 2A

Provisional projection (Brodmann's area, BA)	Which mental function is connected with	The number of TCMP administered	
		group 1 ($n = 38$)	group 2A ($n = 62$)
The left hemisphere			
BA 44, 45	The motor speech center (Broca's area)	45	131
BA 42	The sensory speech center (Wernicke's area)	46	112
BA 43	Central representation of articulation	26	55
BA 6–8	Central representation of the hand and the function of writing	21	43
BA 22	Phonemic hearing zone	14	30
BA 9, 40, Area 37-39-19 TPO-boundaries	Associative divisions of the frontoparietal region	17	81
A total of TCMP per left hemisphere		169	452
The right hemisphere			
BA 42, 44, 45, 22	Broca's and Wernicke's areas	8	10
BA 9, 37-39-19	Associative zones of the frontoparietal divisions	8	49
A total of TCMP per right hemisphere		16	59
Total		185	511

The analysis of the characteristics of cortical rhythmicity in the children studied revealed the immature EEG type in the form of the absence of or incomplete formation of the occipitoparietal focus of the main α-rhythm in 77% of cases [9, 19].

The data of the pilot MRI-aided brain studies conducted prior to the course of TCMP in part of the children showed that for the labels (which, supposedly, corresponded to the projections of the cortical HMF centers), the discrepancy with Brodmann's area (BA) boundaries determined by MRI and converted to the coordinates of the stereotactic atlas constituted from 1.9 ± 1.9 mm (BA 44–45) to 8.6 ± 3.3 mm (BA 8) and 12.9 ± 9.8 mm (BA 42). However, these values did not go beyond the diameter of the electrodes and padding (30 mm) used, which allowed us to employ Krenlein scheme with a known error when we chose the exposure targets without resorting to compulsory MRI prior to the beginning of the TCMP course (since children with a delay in mental and speech development are subjected to it under anesthesia).

An exceptionally important role of speech in the formation of child psyche underlay the choice of the provisional cortical projections of the motor and sensory speech centers as the primary targets of TCMP exposure in preschool children.

As seen in Table 3, in group 1 (children with speech development disorders but with normal development of the other HMF), the main share of TCMP was near the cortical projections of the left hemispheric Brodmann's areas 44–45. In the presence of an obscure form of dysarthria and/or a low-level development of fine (hand) motor skills, TCMP on the cortical projections of areas 43, 6–8 were also included in the exposure scheme. The range of exposures of the cortical projections in the right hemisphere was minimal.

When we drew up the TCMP program for group 2A children (with a combined delay in HMF and speech development, with no autistic symptoms), tDCS was predominantly provided near the cortical projection of Broca's area with a simultaneous increase in the number of TCMP on the provisional cortical projections of the associative regions due to a larger number of older preschool children in this group (Table 3).

In group 2B and 2C children with a combination of HMF and speech disorders with autistic symptoms, the predominant exposure of the cortical projections of the speech zones to TCMP in preschool age was preserved but shifted to the area 42 projection (Wernicke's zone) (Table 4).

The analysis of the HMF and speech changes in the groups of children examined during TCMP is shown in Table 5. It is seen that in group 1 children predominantly with speech disorders, changes in block II (speech) are most markedly pronounced according to the TCMP correction scheme. One or two TCMP sessions (20 min each) resulted in better understanding of the speech addressed, the enlargement of an active and passive vocabulary, the improvement in the prosodic speech components, etc.

In children with a combination of HMF and speech retardation, positive changes were less marked

Table 4. Provisional TCMP targets in schoolchildren with autism spectrum disorders in groups 2B and 2C

Provisional projection (Brodmann's area, BA)	Which mental function is connected with	The number of TCMP administered	
		group 2B ($n = 42$)	group 2C ($n = 29$)
The left hemisphere			
BA 44, 45	The motor speech center (Broca's area)	76	41
BA 42	The sensory speech center (Wernicke's area)	109	103
BA 43	Central representation of articulation	15	3
BA 6–8	Central representation of the hand and the function of writing	15	20
BA 22	Phonemic hearing zone	2	4
BA 9, Area 37-39-19 TRO-boundaries	Associative divisions of the frontoparietal region	33	15
A total of TCMP per left hemisphere		250	186
The right hemisphere			
BA 42, 44, 45	Broca's and Wernicke's areas	17	6
BA 9 BA 37-39-19	Associative zones of the frontoparietal divisions	28	22
A total of TCMP per right hemisphere		45	28
Total		295	214

Таблица 5. Положительные изменения в психическом развитии у детей под влиянием ТКМП

Groups of children	Blocks of psychological parameters (by the increase in significant changes at $p < 0.01$—from left to right)			
1—speech disorders with normal HMF	behavior IV	HMF III	activation I	speech II
2—combined HMF and speech disorders	IV	III	II	I
2A—without autistic symptoms				
2B—with autistic symptoms	IV	III	I	II
2C—early infantile autism (EIA)	IV	I	III	II

in block IV of complex functions (voluntary types of activity, verbal regulation of behavior, etc.) and increased in blocks I–II (activation, speech). It is noteworthy that, in the presence of autistic disorders, the dynamics was predominantly observed in relation to impressive speech. According to the ADOS questionnaire data, after TCMP, children with autistic spectrum disorders were transferred from the severe autism category to the mild or moderate autism category (Table 6).

The Woodcock–Jonson scale data also demonstrated a significant improvement in the whole number of mental functions of children with autistic spectrum disorders: in the fine motor skills, social integration, speech comprehension, and speech and learning habits scales (Table 7). In particular, the quality of looping

Table 6. Dynamics of the development of children with autism spectrum disorders treated with TCMP

Before the course of TCMP ($n = 29$)		After the course of TCMP	
average ADOS values (score)	the degree of autism	average ADOS values (score)	the degree of autism
42.5 ± 7.7	Severe	32.6 ± 6.6	Moderately severe (mild)

Table 7. Acquisition of social habits in children with developmental autism spectrum disorders treated with TCMP

No.	Woodcock--Jonson subscale	Average relative parameter values (%)	
		before the course of TCMP	after the course of TCMP
1	General motor skills	41 ± 7	42 ± 7
2	Fine motor skills	32 ± 6	37 ± 7**
3	Social communication	12 ± 6	19 ± 7**
4	Speech comprehension	13 ± 5	20 ± 5**
5	Speech habits	13 ± 9	20 ± 10**
6	Eating behavior	29 ± 4	30 ± 5
7	Using a toilet	40 ± 13	43 ± 12
8	Dressing	31 ± 8	33 ± 8
9	Self-care	22 ± 8	24 ± 8*
10	Practical home experience	14 ± 9	16 ± 9
11	Time	5 ± 4	5 ± 4
12	Money	4 ± 3	5 ± 3
13	Learning habits	7 ± 3	11 ± 3**
14	Spatial orientation	12 ± 4	13 ± 4

* $p < 0.05$, ** $p < 0.01$.

and shading improved when they worked with a pencil; more careful handling with small objects and the appearance of a subject drawing were observed. An increase in productive activity was also observed: the possibility of choosing and sorting objects, the use of tools, a change in the intensity of work if necessary, etc. The children began to participate in joint activities, to use personal pronouns, to show initiative when seeking out counterparts to communicate with; they showed more interest in their peers, and the duration of visual contact increased. The changes described began to show up as early as in the first and second week when they underwent the TCMP course, with a positive effect being further increased on completion of the course.

DISCUSSION

The results obtained demonstrate that the structural changes visualized (by means of MRI) in the brain of the preschool children might not underlie mental disorder associated with residual organic background (as a consequence of organic CNS damage of perinatal origin). In 70% of cases, children with these disorders have normal age-specific characteristics of the brain structures or slight changes of posthypoxic origin. This indicates the possibility of a discrepancy between the degree of structural and functional disorders of cerebral activity and the actual level of mental development of a child and sets special requirements for the elaboration of the neurophysiological criteria of developmental disorders, early biological markers of HMF and speech disorders [23].

Earlier, we showed that the presence/absence of the occipitoparietal focus of the EEG α-rhythm with the eyes closed could be used as one of such criteria [9, 19]. In particular, a significant increase in the rate of occurrence of the immature EEG type (without this focus) was established as the degree of delay in development increased, as well as with a low effectiveness of the conventional methods of correction. Whereas the immature EEG type in children with a combined delay in the development of HMF and speech who underwent TCMP and were examined by us in 2004–2008 accounted for 61% [19], in the 2010–2013 sample, it was as high as 77%.

Not being an absolute physiological criterion of retardation of mental and speech development, this parameter of EEG immaturity can be used as a probability (risk) marker of such a delay at the early stages of ontogeny. This is important because, as shown by the data of our longitudinal studies, the EEG type (the visual pattern with the presence/absence of the occipitoparietal α-rhythm focus) is most likely to be preserved with age and may therefore be an important prognostic sign [9, 19].

The predominance of functional rather than structural disorders of cerebral activity in children lagging behind is the physiological basis of the effective application of directed brain exposure to local TCMP. The presence of relatively intact links of the brain systems ensuring the motor, speech, associative, and other functions (if we are to use Bechtereva's terminology [24]) aids over sufficiently short periods (days, weeks from the moment of exposure) in the actuation or facilitation of the physiological processes owing to

which the more or less formed function established in ontogeny evolves from a nonworking to working state. This could be observed in group 1 children with delayed speech development and general speech underdevelopment that were not accompanied by retardation of other HMF. But for an immature function to be formed or a compromised mental function to be restored, as in group 2 children, a longer time interval is, undoubtedly, needed when the formation of new functional relationships is stimulated by TCMP [9, 25].

As shown by our investigations, TCMPs are also a fine neurophysiological tool for studying the characteristics of mental and speech development of a child at different stages of ontogeny. In particular, a shift in the predominance of TCMP to the projections of the left hemispheric speech centers (Broca's and Wernicke's areas) at the ages 3–5 years considerably facilitated the attainment of an increased level of speech development, both impressive and expressive speech. This probably occurred due to an activation of congenital language systems.

In cases when the delay in development is more obvious, the positive dynamics develops at a slower rate (apparently, due to damage to the initial language matrices of memory) and requires repeated TCMP courses. For example, in children with autistic spectrum disorders the appearance of expressive speech underwent certain stages, which were not actuated in the process of natural ontogeny. Positive shifts in this group began with impressive speech in the form of the appearance/shortening of response to one's own name, extending the range of understanding requests and instructions. What occurred then was the appearance of echolalias and an increase in their number followed by switching over from speech in the third person singular to the first person. As any artificial process, substituting ontogeny (owing to the use of TCMP) is inferior to the process of natural development of the established speech programs of a healthy child in speed and quality. However, in any case, the effect of the use of TCMP develops systemically owing to both the retained intact structures and connections and the new functional systems formed in the plastic child brain.

However, the development of stimulated HMF proceeds at a high rate only near the sensitive periods of development of certain mental functions. Beyond them, the substitution rate is significantly slower. In other words, the older the child, the more slowly the processes of substituting ontogeny occur making an effective correction of disturbed functions impossible, despite the structural integrity of the brain formations (according to MRI findings).

The process of development of changes in the mental activity of an abnormal child and his or her social adaptation in the course of therapeutic TCMP naturally depends on many other factors as well: the severity of the initial pre- and perinatal impairment of the nervous system leading to damage or underdevelopment of one or another brain structure, the degree of plasticity of the child brain and its biological resource, the features of the developing environment as well as the adequacy of age-related loads.

CONCLUSIONS

(1) The signs of changes in the brain structures of children with a delay in mental development due to organic CNS damage of perinatal origin are visualized during MRI in less than in 30% of cases at a preschool age, whereas the share of immature EEG (with unformed occititoparietal α-rhythm focus) accounts for 77% in this group of children.

(2) The predominance of the signs of functional disorders in the groups of children studied is the physiological basis for increasing the effectiveness of TCMP. The exposure near the projections of the cortical centers of speech, the motor and associative types of activity allows us to stimulate the functional potentialities of intact components of the brain systems ensuring mental activity (established during ontogeny) or to contribute to the formation of new functional relationships and systems instead of those damaged in the perinatal period.

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