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Age-Related Characteristics of Brain Development in Children Living in the North

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The morphofunctional age-related development of the brain was studied in schoolchildren living in the difficult climatological-geographic and socioeconomic conditions of the north (Arkhangel'sk region). Of the 62 students in country middle schools, EEG amplitude-frequency, time, and spatial measures corresponded to age norms (European norms) in only 10 cases (16%). A further 26 children (53%) showed minor abnormalities in the form of an inadequate degree of organization of the temporospatial EEG pattern, mainly in the frontal and temporal lobes of the brain, with increases in the levels of the theta and delta rhythms, and the absence of any marked "functional nucleus" in the alpha rhythm. In the remaining 14 children (29%), EEG measures showed more marked delays in mental development (DMD), which were combined with learning difficulties and abnormal behavior. The retardation in the morphofunctional development of the brain in northern children averaged 1.5–2 years, which coincides with delays in hormonal and physical development described by other authors.

KEY WORDS: north, children, brain development.

A whole series of factors acts on humans in the conditions obtaining in the north, these not only increasing the demands on physiological systems but also affecting the rate of the morphofunctional development of the body. Assessment of physiological measures in developing humans requires identification of age norms allowing determination of whether one or another variation in measures of functional systems is a pathological sign or results from a developmental delay associated with living in the north.

The search for objective criteria for evaluating the periods of brain development in children and the formation of integral systems activity is a current topic in age physiology. The most important objective measure of brain function and its functional state is the EEG. Many authors have shown that EEG measures obtained from structural analysis of EEG traces have high prognostic value in identifying the symptoms of functional immaturity of the brain.

Significant rearrangements in the bioelectrical activity of brain structures occur during ontogenesis. School age is of interest to many investigators, especially because systematic learning occurs from age seven years such that the correspondence of the brain to age-related needs becomes of primary importance and determines the success with which knowledge is assimilated [1, 6]. Frid has reported spectral analysis of EEG traces from different areas of the cortex in children aged 7–9 years [12]. These data show that by age seven years, the mean frequencies of the alpha rhythm are 8.7 Hz in the occipital area and 8.1 Hz in the frontal area. Significant changes in the spectral-correlational parameters of the EEG occur at age 8–9 years. The mean alpha-rhythm frequencies are 9.6 Hz in the occipital area and 9.1 Hz in the frontal area. Describing the spectral characteristics of school-age children, the authors noted stabilization of the leading alpha rhythm by 8–10 years, with displacement of its mode to around 10 Hz, i.e., as in adults. However, high-amplitude theta waves were increasingly marked in the anterocentral areas; isolated delta waves could be seen; slow-wave activity was encountered in the

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posterior areas [10]. After age eight years, the alpha range became the main activity in the process of attention, and the frequently encountered theta and delta waves were not considered pathological.

An important aspect of assessment of the morphofunctional maturation of the body relates to the times of sexual maturation. Formation of the mature type of regulation of reproductive functions occurs with the establishment of the neuroendocrine system. Thus, qualitative evaluation of the stage of sexual maturity based on the extent of secondary sexual characteristics accords well with division of the development of the endocrine system into stages.

Thus, the main aim of the present work was to assess the levels of age-related brain development in northern children in terms of the structure of the pattern and spatial organization of overall bioelectrical activity (the EEG).

METHODS

The effects of the climatological-geographic, biogeochemical, and social conditions of the northwest region of Russia on the level of physical and mental development of children were addressed by four scientific expeditions in the Konoshskii area of the Arkhangel'sk oblast (at different seasons of the year). Complex medical-physiological studies were performed four times using students in classes 1–11 in country middle schools.

The state of the central nervous system was assessed by multichannel computerized EEG recording. EEG traces were recorded with subjects lying with the eyes closed, from the posterofrontal, mid-temporal, parietal, and occipital areas (F3, F4, T3, T4, P3, P4, O1, O2) using the international 10–20 scheme, with recordings made using a Telepat-104 computerized EEG. Causes for developmental abnormalities were sought by taking detailed histories from the parents, with the aim of identifying pathological events in pregnancy and delivery, including birth traumas to the children, subsequent illnesses and traumas, the occurrence of harmful habits and drug addiction in the parents, etc.

Mathematical data analysis was performed using an original set of computer programs (for EEG brain mapping, algorithmic analysis of interactions between rhythmic components of brain bioelectrical activity, intrahemisphere and interhemisphere interactions), providing qualitative and quantitative assessments of the level of morphofunctional age-related development of the central nervous system with stratification by age and gender, along with identification of individual characteristics of age-related development and deviations from normal. The children simultaneously underwent psychoneurological investigations.

EEG analysis in each lead included assessment of the amplitude, frequency, and indexes of the delta, theta, alpha, and beta rhythms. Fourier analysis was used to evaluate spectral power density.

Studies of brain bioelectrical activity in children with delayed mental development were directed to identifying the degree and nature of EEG deviations from age norms, assessing pathological changes in biopotentials and their locations, and determining the relationship between EEG data and clinical-neurophysiological measures of DMD. Data were analyzed statistically using Statistica for Windows.

RESULTS AND DISCUSSION

Analysis of the formation of the various EEG measures in the study children demonstrated the non-linear nature of their changes with age. Thus, the fastest increase in the alpha rhythm in boys and girls was seen in the period from 13 to 14 years, while there was some decrease in the alpha rhythm index from 14 to 15 years of age (Fig. 1). During this period, boys showed a decrease in the rate of decrease of the theta rhythm index, while girls could show some increase. Many authors have linked this increase in the proportion of slow rhythms (resembling an EEG "regression") with the hormonal rearrangements occurring at this age [11, 16].

Many studies have demonstrated the topographic characteristics of EEG rhythm establishment, characterized by the earlier formation of the "adult" type of activity in the occipital areas and some delay in the central and frontal areas [11, 13]. The age of 9–10 years, when the baseline EEG is characterized by hypersynchronous polyrhythmic alpha rhythms with an appropriate regional distribution, is an important stage in the pathway to establishing systems activity in the child's brain [2, 3]. The pubertal period is

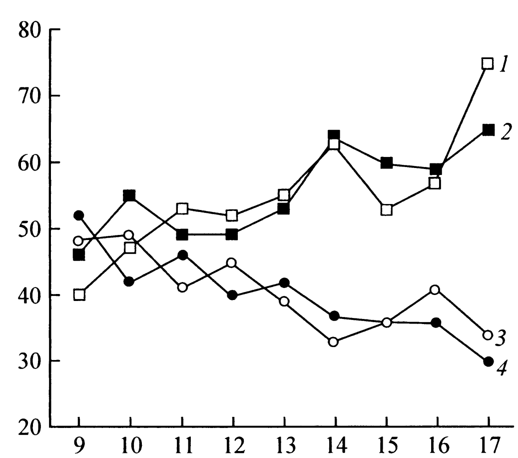

Fig. 1. Age-related rearrangements in the extents of EEG rhythms in school students living in the Arkhangel'sk region. The abscissa shows age, years; the ordinate shows the EEG rhythm indexes, %. *1*) Age-related dynamics of the α rhythm in girls; dynamics of the α rhythm in boys; *3*) dynamics of the θ index in girls; *4*) dynamics of the θ index in boys.

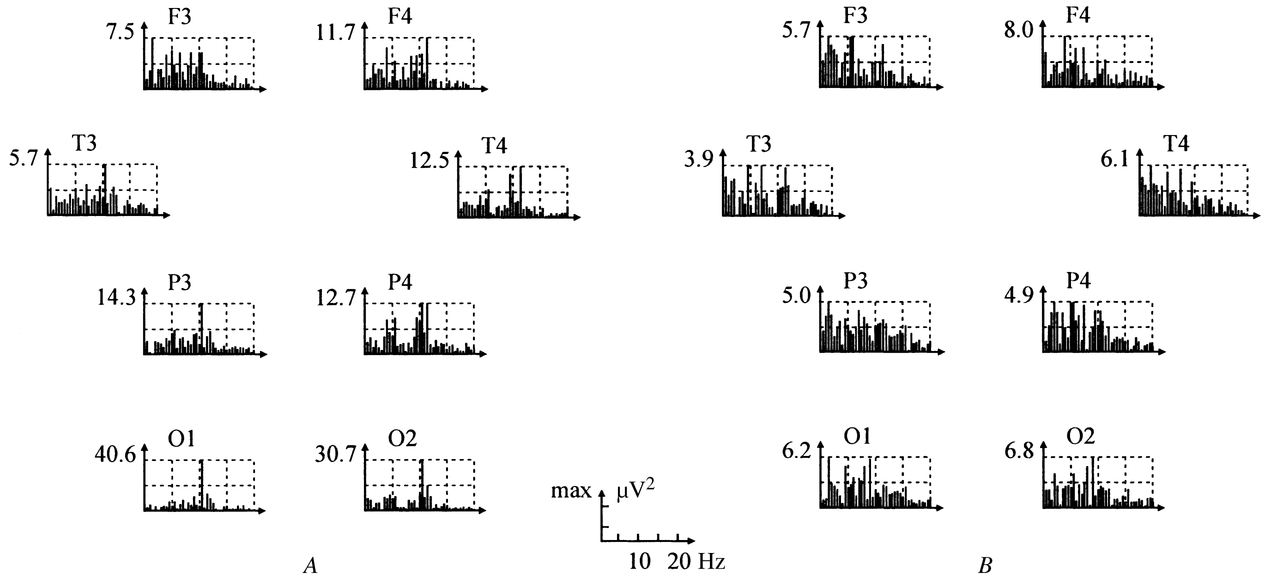

Fig. 2. EEG power spectra in children with normal age-related development (*A*) and marked delay in mental development (*B*). F3...O2 show EEG leads according to the international 10–20 scheme.

characterized by some "regression" of the EEG: large numbers of slow theta waves appear and the leading alpha rhythm slows somewhat (by 0.5 Hz) [7]. According to Farber and Dubrovinskaya [11], school age involves a heterochronous establishment of various subranges of the alpha rhythm: the alpha-1 rhythm (7–9 Hz) reaches maximal power at 7–8 years in the caudal areas of the brain; the alpha-2 rhythm (10 Hz) dominates after age 10 years and allows more extensive integration between centers; establishment of the alpha-3 rhythm (11–13 Hz) occurs later and facilitates the formation of local functional constellations. The immature type of cortical activation, with a smaller number of components, is gradually replaced by the mature type of activation. This also involves thalamic structures; generalized activation is accompanied by localized activation of individual elements of the system, etc.

The results obtained here showed that of 62 middle school students, only 10 (16%) fully met European age norms for EEG characteristics. In 38 children (61%), there were minor deviations, with inadequate levels of organization of the temporospatial EEG pattern, mainly in the frontal and temporal parts of the brain, increases in the levels of the theta and delta rhythms, and the absence of clearly marked "functional nuclei" [9] in the frequency range of the major rhythm (the alpha rhythm), reflecting the optimal nature of interactions between centers.

Figure 2 shows an example of the spectral analysis of the EEG in children aged 10 years with normal development (*A*) and with delayed mental development (DMD) (*B*). The EEG spectrum of a child with normal age-related development shows a predominance of spectral power in the alpha range, with a dominant frequency of 10.2–10.4 Hz. The EEG of a child with delayed mental development showed spectral power density predominating in the delta and theta ranges. These differences were also apparent in the zonal distribution of the alpha rhythm. Children with normal development showed a focus of alpha activity in the occipital areas, while alpha rhythm power in other areas was significantly lower. Children with delayed age-related development showed smoothing out of differences in alpha rhythm power. Comparison of the spectral topograms of children with normal development with those of children with minor and major developmental delays showed that these differences had their greatest effects on the slow EEG rhythms – the theta and delta rhythms. The magnitude of these effects increased with increases in the extent of morphofunctional brain developmental delays.

Studies of the EEG in the state of calm waking in children aged 8–9 years with DMD showed abnormalities in baseline EEG rhythms in 40% of cases, with low-amplitude disorganization of the alpha rhythm, with displacement of the focus of maximal expression from the occipital area to the parietal and frontal areas. The alpha rhythm was often seen as rare isolated groups – so-called alpha-rhythm fragments. Some cases showed high-amplitude bilaterally synchronized theta-rhythm discharges in the frontal and temporal areas of the hemispheres, amplifying and generalizing on hyperventilation.

Nahas and Krynski [14] suggested that the greater extent of the theta rhythm in children with learning difficulties reflects immaturity of brain structures. In children with delayed mental development of organic cerebral origin, some 50% of cases showed EEG changes demonstrating organic lesions of diencephalic structures and the cerebral cortex [4].

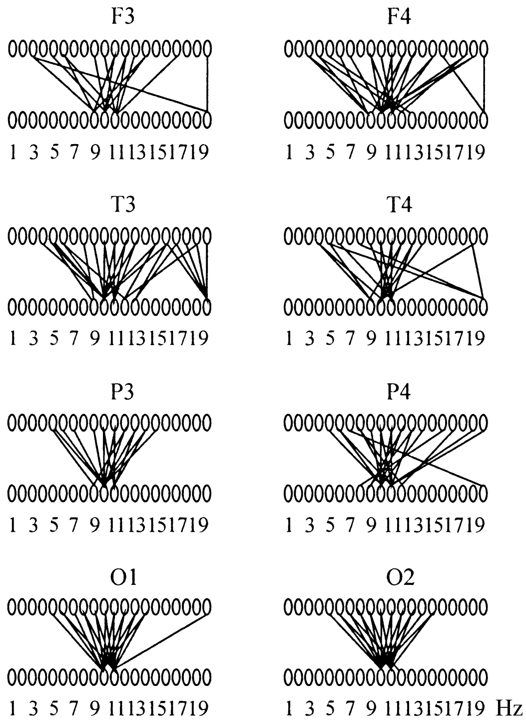

Fig. 3. Characteristics of algorithms for the temporal organization of EEG patterns in children with normal rates of age-related brain development. F3...O2 show EEG leads according to the international 10–20 scheme. Circles and numbers 1–19 beneath them show EEG frequencies in Hz; the upper row of circles shows the preceding EEG wave, the lower row shows the following (current) wave. Lines show transfers from one wave in one frequency range to waves in the same or a different range over an analysis epoch of 2 min.

Marked abnormalities in the nature and structure of brain bioelectrical activity, providing evidence for delays in age-related development and the accompanying learning and behavioral problems, were seen in 14 children (23%). Relative delays in age-related development in this group of children averaged 1.5–2 years. Maternal histories in this group of children showed that the possible causes of the delay might include complications during pregnancy, and difficulties with delivery associated with neonatal hypoxia, as well as originating from socially disadvantaged families, all of which hinder normal child development.

This raises the question of whether the delay in age-related morphofunctional development in northern children is characteristic only of the brain or is a reflection of slower rates of maturation of all body systems in children living in the specific climatological-geographical and socioeconomic conditions of the northern regions.

Comparison of the ages and stages of sexual development as defined by Tanner [17] in this group of children performed in the same expeditions by colleagues at the Institute of the Physiology of Natural Adaptation, Urals Branch, Russian Academy of Sciences [5] showed that study children of the same age (within one year) were at different stages of sexual development. Comparison of the stages of sexual development with data obtained in the Moscow region [8] provided evidence that the proportion of children of a given age group at higher stages of sexual development was greater in the Moscow region than in the Arkhangel'sk region. Thus, at age 15–16 years, 100% of study girls were in the fourth stage of development, while only 10% in the Moscow region were at this stage, the remaining 90% being at stage 5. Comparison of the other age period showed that children living in the country in the Arkhangel'sk region, as compared with the Moscow region, showed delays of 1–2 years in sexual maturation.

Sil'verova and Filippova [8] analyzed more factual data in their studies of the dynamics of secondary sexual characteristics in 499 girls and 322 boys in the Moscow region and concluded that the distribution of study children by stage of sexual development showed high variability for a given age. These conclusions were also supported by data obtained in northern children, with the difference that sexual maturation in the latter occurred more slowly in all age groups [5].

The principle of the integral (systems) organization of brain activity suggests a dynamic coordination between all bioelectrical processes. While analysis of the amplitude-frequency spectra of EEG traces allows assessment of the maturity of individual cortical and subcortical brain structures, formation of systems regulatory functions is reflected in algorithms for the interaction of the major EEG components (waves), their temporal and spatial organization, and the characteristics of dynamic rearrangements when the type of activity being performed changes [3, 9]. These are clearly shown in the dynamics of intrahemisphere and interhemisphere interactions, assessed using correlation and coherence relationships, and leading phase relationships of the main rhythms of bioelectrical activity in different parts of the brain. We have previously demonstrated that the age-related establishment of the temporal organization of the EEG pattern in children is delayed as compared with the amplitude-frequency characteristics [3, 7].

Figure 3 shows the interaction of the wave components of the EEG (delta, theta, alpha, beta) in children with normal morphofunctional brain development. This shows that the structure of the EEG pattern was well organized in all brain areas in a child with normal age-related morphofunctional development, the major sequence of transitions occurring in the alpha rhythm, i.e., the alpha rhythm was the "functional nucleus" organizing the interaction algorithm between all EEG components. The structure of the interaction of components in the EEG pattern in a child with delayed development (Fig. 4, *A*) showed clear organization, with a "functional nucleus" in the alpha rhythm only in the occipital and parietal areas. In the frontal and parietal areas, this algorithm for the interaction of components was still unformed, evidencing some delay in the morphofunctional

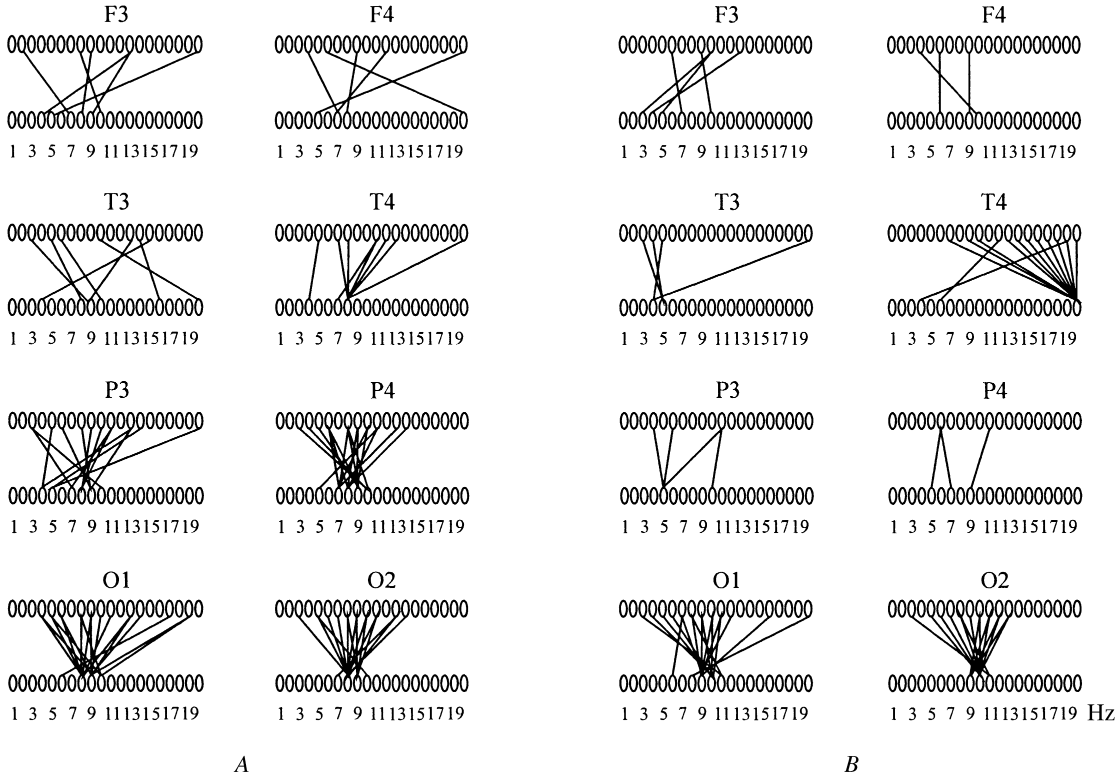

Fig. 4. Characteristics of algorithms for the temporal organization of EEG patterns in children with minor delays in age-related development (*A*) and marked delays in development (*B*). For further details see caption to Fig. 3.

maturation of the anterior parts of the brain. In this case, the structure of the EEG pattern in a 14-year-old schoolchild corresponded to the EEG pattern in a child of 12–13 years.

Figure 4, *B* shows a further irregularity in the formation of the algorithm of the interaction between EEG components; the pattern has a normal structure only in the occipital areas. There was a predominance of interactions in the theta and delta rhythms; the right temporal area also showed a beta rhythm, which is evidence for high neuroemotional tension and instability of systemic regulatory mechanisms. In this case, we are dealing with marked DMD with elements of cerebral pathology. Studies of cerebral circulation in this child demonstrated circulatory impairment in the vertebrobasilar basin (predominantly on the right), due to perinatal trauma.

Analysis of the ability of the brain to undergo rapid dynamic rearrangements in relationships between centers is important in assessing the morphofunctional maturity of the brain. This property can be assessed from the time dynamics of the phase leading of rhythms and their correlational relationships. Figure 5 shows data from analysis of the phase leading of rhythms and correlational EEG relationships for all leads. This shows that phase leading of rhythms in a child with normal age-related brain development showed a marked spatial mosaicism both in terms of the phase-coincident rhythms and the leading and lagging phases in different areas (Fig. 5, *I*, *a*, *b*, *c*). This is evidence for the marked dynamic nature of intracortical processes, their interconnections, and constant substitution of leading in different brain zones in supporting and maintaining systems activity in the whole brain. This transition in leading in particular brain zones is shown by the numbers on the recording channels shown in Fig. 5, *I*, *B*, *a*. In a child with marked impairments in age-related brain development, this variation in the phase leading of rhythms in different brain zones was virtually absent, and bioelectrical activity in different brain zones coincided in phase (Fig. 5, *II*, *A*, *a*, *b*, *c*), which is evidence for the existence of powerful core organizing influences. While interhemisphere interactions dominate in normal brain development (Fig. 5, *I*, *B*), this predominance was seen for intrahemisphere connections in conditions of marked delay (Fig. 5, *II*, *B*).

This nature of local and spatial rearrangements in the EEG amplitude-frequency spectrum, the structure of interactions between the wave components, and their dynamics reflect the gradual morphofunctional maturation of the brain as a system and the formation of interactions between centers, which ultimately support specific self-regulatory mechanisms, the coordination of intersystems interactions at different age stages of child development

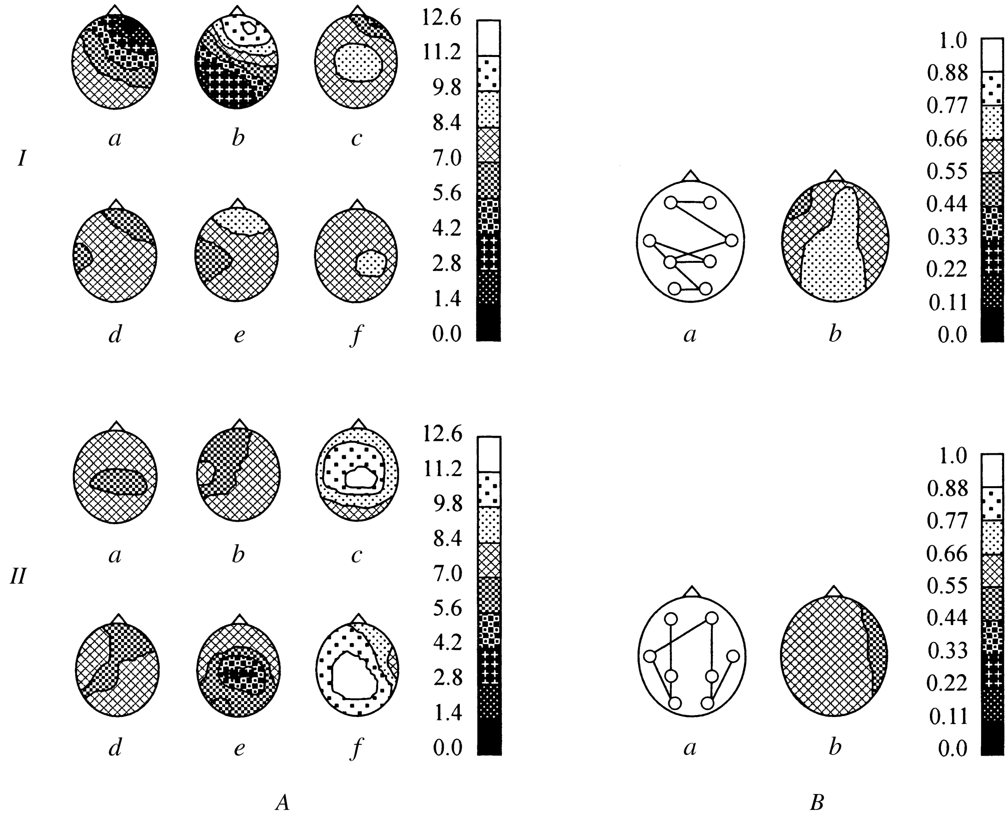

Fig. 5. Topograms showing leading phase and correlational relationships in EEG recordings from different brain zones in children with normal age-related development (*I*) and with developmental delay (*II*). *A*) Leading phase topograms: *a*, *d*) phase leading; *b*, *e*) phase lagging; *c*, *f*) phase coincident. The upper row of topograms was obtained using an analysis epoch of 4 sec, the lower with an analysis epoch of 20 sec. The scale on the right shows the phase time shift, msec; *B*) correlational relationships between EEG leads: *a*) phase time shifts; *b*) topograms showing significant correlation coefficients. The scale on the right shows values for the correlation coefficient.

directed to maintaining viability, and adaptation to the environment.

The existence of "disorganized" and "poorly organized" EEG patterns in schoolchildren is evidence that relationships between centers supporting systems activity in the whole brain are unstable in these children, while brain structures responsible for generating the major rhythms of bioelectrical processes are incompletely formed and still have no stable dynamic interactions between them, preventing achievement of the optimum level of perception of information from the environment. The brains of these children show more variable responses to external signals, though the instability of intrahemisphere, interhemisphere, and cortical-subcortical interactions prevents prolonged concentration on defined types of activity and hinders the perception of new information, which is often accompanied by inappropriate behavioral responses. This type of organization of the central nervous system facilitates the appearance of interpersonal conflicts because of the inability to assimilate learning loads; this leads to increased neuropsychological tension and excessive neuroticism and, in some case, depressive states. It should be noted that some delay in the morphofunctional development of some children living in the countryside of the northern territories should not be regarded as pathological, being associated with the later (as compared with the central band of Russia) development of hormonal, immune, and other visceral systems and the lower informational loading on the brain. Analysis of the structure of successes (allowing for subject), mental activity, and general behavior provides evidence that the level of activation of cortical structures in the first and second groups of school students is sufficient for them to cope with current school programs and adapt adequately to their environment. The first group (18%) could support significantly greater learning loads. As regards children with marked developmental delay, active intervention is required for correcting these impairments. One effective method for modulating relationship between centers in DMD is adaptive biocontrol with feedback from EEG parameters in combination with metabolites and general reinforcing therapy.

Thus, the results obtained from medical-physiological studies in the Arkhangel'sk region showed that the complex of heliogeophysical, climatological, technogenic, and social conditions obtaining in the northwest region of the Russian Federation has specific effects on the physical and psychophysiological age-related development of children, consisting of a shift in the timing of sexual maturation to a later age and a later (as compared with average European norms) age for the formation of the morphofunctional organization of the brain.

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