DOI 10.1007/s11055-014-9999-x
Neuroscience and Behavioral Physiology, Vol. 44, No. 8, October, 2014

Comparative Studies of EEG Theta and Gamma Rhythms in Normal Children and Children with Early Childhood Autism

E. A. Lushchekina,[1] E. D. Podreznaya,[2] V. S. Lushchekin,[2] V. Yu. Novototskii-Vlasov,[1] and V. B. Strelets[1]

UDC 612.821+612.822.3

Translated from Zhurnal Vysshei Nervnoi Deyatel'nosti imeni I. P. Pavlova, Vol. 63, No. 4, pp. 451–459, July–August, 2013. Original article submitted June 27, 2012. Accepted February 11, 2013.

We present here a comparative analysis of spectral power and mean coherence of the theta and gamma rhythms in healthy boys and boys with early childhood autism aged 5–7 years (mean age 6 years 1 month) in the state of rest and on cognitive loading (counting). In contrast to the situation in patients, the background theta rhythm in healthy children showed a marked fronto-occipital gradient. In early childhood autism, the spectral power of the theta rhythm in baseline conditions had lower values than in healthy children, while baseline gamma rhythm power was greater. In healthy children, cognitive loading led to decreases in spectral power and mean coherence in the theta rhythm and increases in these measures of the gamma rhythm. In patients with early childhood autism, cognitive loading produced no marked changes from baseline in either rhythm. In healthy children, counting shifted the focus of theta-rhythm activity to the right occipital area, which did not occur in patients with early childhood autism.

Keywords: cognitive tests, early childhood autism, EEG spectral power.

Previous studies [7, 8] have addressed the question of the extent to which EEG characteristics typical of adult schizophrenia patients apply to children with early childhood autism (ECA). It has become possible to state the problem in these terms since clinical studies of ECA demonstrated that positive symptoms could arise and that ECA could develop into a processual disorder of the schizophrenia type [1]. Many children with ECA are diagnosed with "schizophrenia" at age 7–8 years. We were interested to determine whether EEG data could be used to obtain early information regarding the probability of this change in diagnosis. Published views on this question are contradictory, while solution of the problem is very important for the timely provision of corrective and rehabilitation services. Definition of the possible criteria for the development of ECA into schizophrenia based on EEG data are of great scientific and social significance. Despite the specific features of cognitive impairments in ECA associated with the characteristics of information processing [19] and interhemisphere interactions [25], similarities in the mechanisms of these two types of pathology can be suggested [22]. Studies have shown [7, 8] that cognitive loading in healthy children produces increases in the spectral power and coherence of fast rhythms from baseline levels. In early childhood autism, the spectral power of the alpha rhythm decreases, while the spectral power of the gamma rhythm is higher than normal, including in baseline conditions. Cognitive loading of patients produces smaller changes in the spectral power of fast rhythms than seen in normal subjects. Decreased alpha-rhythm power is seen in children with autism and in adults with schizophrenia, with both positive and negative symptoms [13]. Similar changes have also been described in adolescents with schizophrenia spectrum disorders [3]. The increased spectral power of the

[1] Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences; e-mail: elena.luschekina@yandex.ru.
[2] Department of Developmental Psychophysiology, Strogino Psychological-Pedagogic Rehabilitation and Correction Center, Moscow.

fast rhythms in baseline conditions seen in our studies in children with early childhood autism is also characteristic of schizophrenia with positive symptoms, and the decreased reactivity of the fast rhythms demonstrated in affected children by our studies in response to cognitive loading has been described for schizophrenia with negative symptoms [13]. The fact that the trends to changes in the alpha and gamma rhythms in patients and healthy subjects are in different directions raises the question of how the theta rhythm changes in patients with autism, this rhythm being linked with memory formation and emotional arousal processes and undergoing complex and differently directed changes during normal maturation and during the development of pathological processes [2], as compared with fast rhythms. The presence of theta activity on the EEG in particular conditions may be a sign of pathology affecting diencephalic structures [2]. Some hold the view that the theta rhythm recorded in the central and central-parietal areas in severe autistic disorders may serve as a marker for the severity of the condition [12]. Finally, the question of comparing changes in the theta and gamma ranges is of particular interest, as these rhythms, which are known to modulate each other, constitute an important basis for mental activity [17].

The present study is part of a series of investigations seeking a complex of EEG characteristics which could be used to predict the transfer from childhood autism to schizophrenia. The task was to perform a comparative evaluation of differences in spectral power and mean coherence in the EEG theta and gamma ranges in children with early childhood autism, as compared with normal values and to compare these differences with those described for adults with schizophrenia.

METHODS

Two groups of right-handed boys aged from 4 years 5 months to 7 years 9 months took part in the study: a control group (24 healthy children, mean age 6.05 ± 0.86 years) and a group of children with the diagnosis "early childhood autism," International Classification of Diseases F.84 (27 subjects, mean age 5.79 ± 1.42 years). Subjects were at the stage of initial investigations at the Strogino Psychological-Pedagogic Rehabilitation and Correction Center and had not yet received medication. The parents gave written consent for their children to take part in the study.

EEG recordings were made from 16 electrodes using the standard 10–20% scheme with combined ear electrodes, using a CONAN 4.5 computerized electrophysiological system consisting of a 16-channel amplifier and a personal computer [5]. EEG recordings were made in the frequency range 0.3–70 Hz with a sampling frequency of 256 Hz, a time constant of 0.3 sec, and an analysis epoch of 60 sec. EEG traces were recorded in two conditions – in the resting state with the eyes closed and during mental loading. Cognitive loading consisting of "counting" silently with the eyes closed involved adding or subtracting numbers up to 30. During the experiments, we confirmed that the children did actually do the task required. After standard primary processing procedures, including band filtration to remove network interference and artifacts, data were subjected to secondary processing using programs developed by one of the authors of the present article [11]. Secondary EEG processing included sequential filtration and factor analysis using the "main components" method, which allows artifact-related signals to be selected visually during subsequent transformations. Selected artifact signals were subtracted from the initial unfiltered EEG using coefficients of linear regression. Spectral characteristics were calculated by fast Fourier transformation; mean amplitudes in frequency ranges were subjected to statistical analysis

Spectral power and coherence were studied in the theta (4–7.5 Hz) and gamma (45–65 Hz) ranges. Measures of coherence in individual pairs of leads were averaged as follows: coherence values were initially calculated for each pair of leads in the set used (16 channels). The list of 16 leads gave a number of pairs of $N(N-1)/2 = 120$. Each lead was a member of $N-1$ pairs will all other leads in the list, without repetitions. Mean coherence for all pairs involving a given lead was then calculated for each lead. Use of this parameter allowed results to be presented as isopotential fields rather than a pairs of connections.

Values for spectral power and mean coherence had near-normal distributions, such that parametric statistics methods could be used.

EEG parameters were compared in groups of subjects using unifactorial analysis of variance (ANOVA) [6]. The existence of significant differences between spectral characteristics was accepted at a significance of $p < 0.05$. significance levels of $0.05 < p < 0.08$ were regarded as tendencies to significant differences. The significance of differences for intragroup comparisons (between pairs of electrodes) was assessed using the paired Student's t test.

RESULTS

Baseline spectral power in the theta range in healthy children was maximal in the occipital areas and gradually decreased towards the frontal areas, this being similar to the alpha gradient (Fig. 1). Apart from foci of maximum values, the occipital areas showed a high index of this rhythm in parietal leads *P3* and *P4*. Counting activity led to significant decreases in the mean spectral power of the theta rhythm in all leads as compared with the state of resting waking ($F_{1,30} = 3.7$, $p = 0.001$). Significant intragroup differences between individual leads also indicated dominance of this rhythm in the occipital leads of the right hemisphere in baseline conditions, with dominance in the left hemisphere during counting activity (Fig. 2). The most marked decreases in spectral power were in the occipital ($p(t) < 0.04$) and parietal ($p(t) < 0.05$) areas.

Baseline activity in children with early childhood autism showed no frontal-occipital gradient of spectral

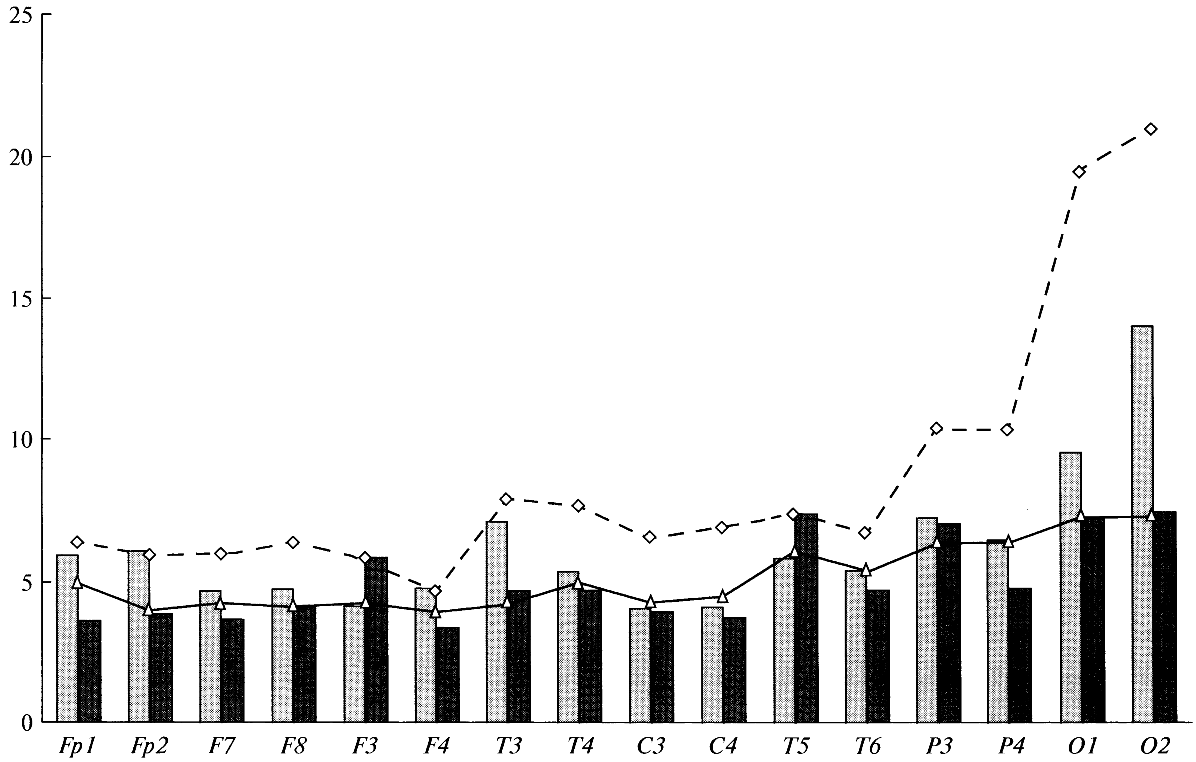

Fig. 1. Spectral power in baseline conditions and on cognitive loading; theta range; comparison of the normal and ECA groups. The ordinate shows spectral power, ∝V²/Hz. The dotted line shows baseline in healthy children; white columns show counting in healthy children; the dotted line shows baseline in patients with early childhood autism; dark columns show counting in children with early childhood autism.

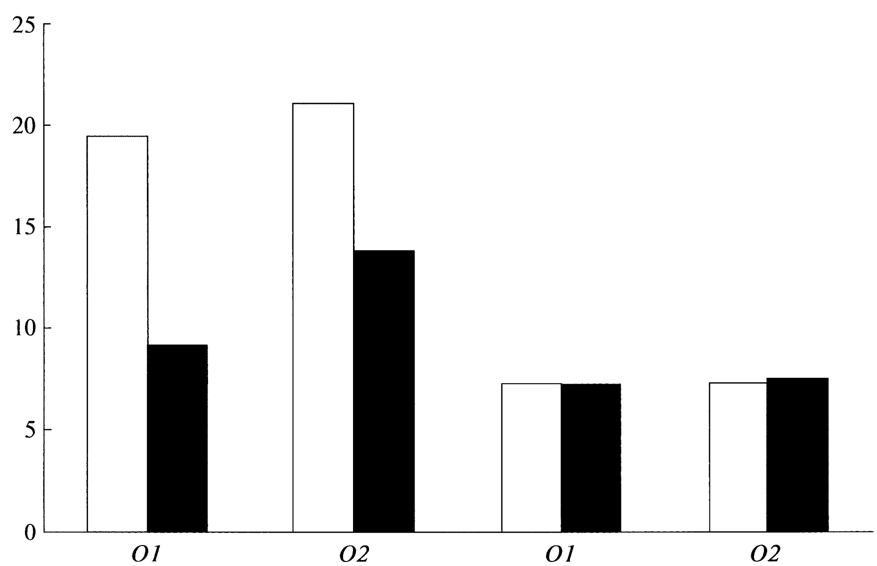

Fig. 2. Spectral power in the occipital leads (*O1* is the left occipital lead, *O2* is the right occipital lead) in baseline conditions and on cognitive loading; theta range; comparison of normal children and children with early childhood autism. White columns show baseline; black columns show counting. The first and second pairs of columns show healthy children; the third and fourth pairs of columns show children with early childhood autism.

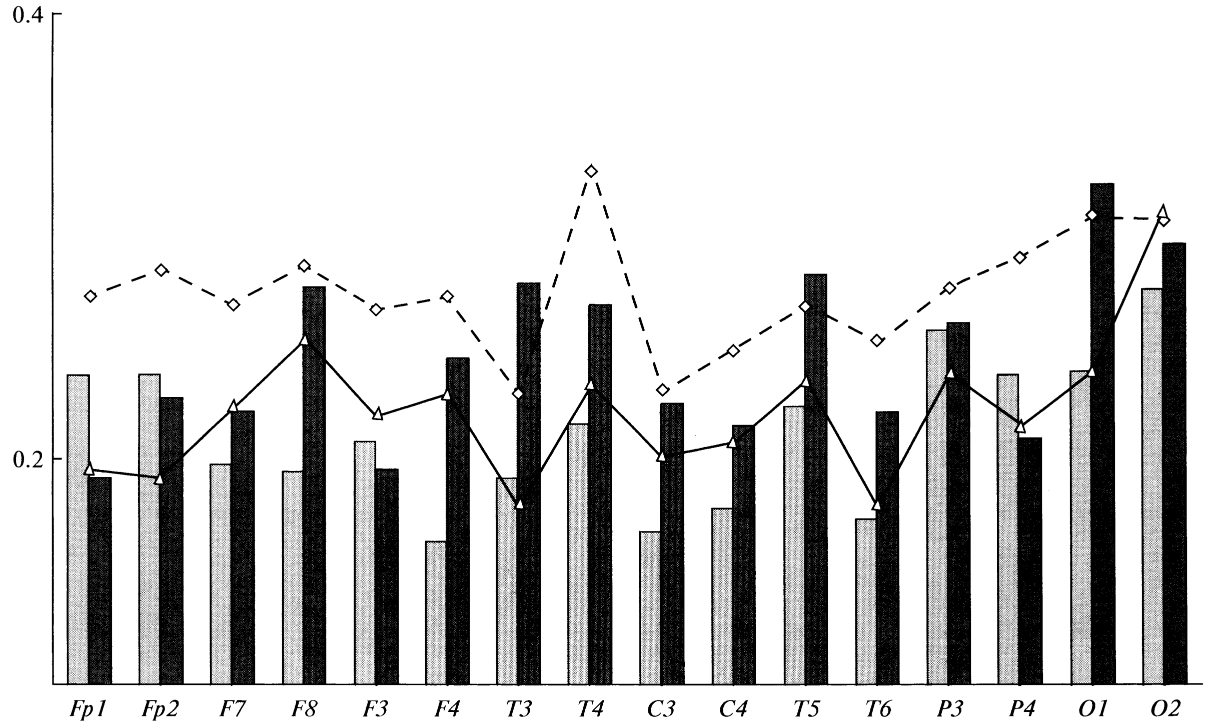

Fig. 3. Spectral coherence in baseline conditions and on cognitive loading; theta range; comparison of normal children and children with early childhood autism. The ordinate shows mean coherence. For further details see caption to Fig. 1.

power in the theta rhythm (Fig. 1). Intergroup differences in power in the baseline EEG in children with ECA were significantly smaller than in children of the control group ($F_{1,30} = 8.66, p < 0.001$). During counting, spectral power in these children showed minor changes (difference from baseline insignificant, $F_{1,30} = 0.156$, $p = 0.872$). However, there were tendencies to increases in theta-rhythm power in the left frontal (*F5*) and left posterior temporal (*T5*) leads ($p(t) < 0.06$ and $p(t) < 0.063$, respectively).

Mean theta-rhythm coherence in healthy children in baseline conditions showed maxima in the occipital areas *O1*, *O2*, in the right anterior temporal area *T4*, and the right frontal band of area *Fp2* (Fig. 3). Cognitive loading altered the distribution of mean coherence: there were significant decreases in the right frontal band (*Fp2*) ($p(t) < 0.005$) in the left anterior temporal (*T5*) ($p(t) < 0.005$) and the left occipital (*O1*) ($p(t) < 0.005$) areas compared with baseline. Mean theta-rhythm coherence in baseline conditions in children with early childhood autism barely differed between leads, though there was a significant reduction compared with the control group ($F_{1,30} = 25.2$, $p < 0.001$). During counting, there was a tendency to an increase in mean theta coherence in the right frontal band (*Fp2*) ($p(t) < 0.076$).

Spectral power in the gamma rhythm in baseline conditions in healthy subjects was maximal in the frontal and occipital areas. Cognitive loading led to increases in spectral power in the frontal, left occipital, left temporal, and left parietal areas ($0.03 < p(t) < 0.05$). Thus, there was a shift in the focus of power to the left hemisphere as compared with baseline conditions. Gamma-rhythm spectral power in autism was significantly higher than in normal subjects; ($F_{1,30} = 12.3$, $p = 0.005$) for intergroup comparison, while on counting there was no significant change compared with baseline ($F_{1,30} = 0.00579$, $p = 0.991$). Intragroup pairwise comparisons (baseline/counting) demonstrated minor ($0.07 < p(t) < 0.093$) age-related increases in gamma-rhythm power in the right frontal polar (*Fp2*), right anterior temporal (*T4*), and posterior temporal (*T5*, *T6*) leads (Fig. 4).

Mean coherence in the gamma rhythm in healthy children on cognitive activity showed higher values than in baseline conditions ($F_{1,30} = 23.1$, $p < 0.001$). Baseline gamma-rhythm coherence in children with early childhood autism was significantly greater than in normal children, with $F_{1,30} = 25.6$, $p < 0.005$ for intergroup differences. On cognitive loading, there was no significant change in coherence in patients. Differences between baseline and counting values were insignificant (Fig. 5).

DISCUSSION

Age-related changes in the EEG during normal development consist particularly of decreases in the representation of low-frequency and increases in that of high-frequency rhythms [2, 4]. The level of representation of the theta rhythm on the EEG in healthy children aged 5–7 years seen

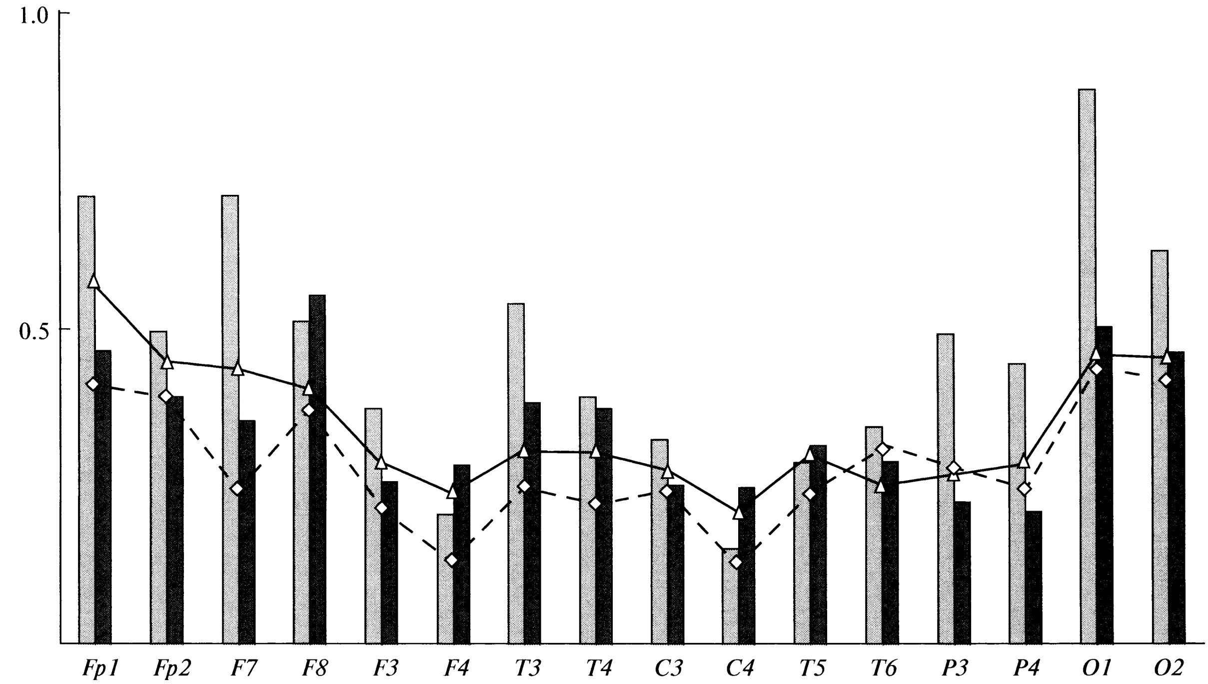

Fig. 4. Spectral power in baseline conditions and on cognitive loading; gamma range; comparison of normal children and children with early childhood autism. For further details see caption to Fig. 1.

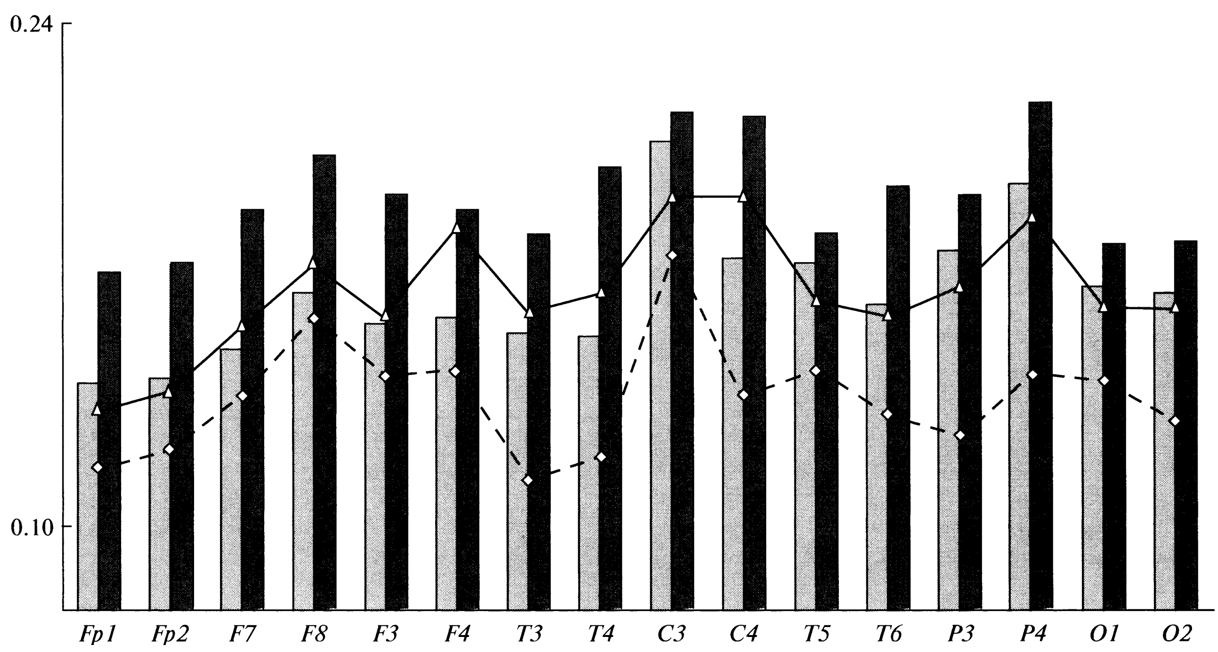

Fig. 5. Mean coherence in baseline conditions and on cognitive loading; gamma range; comparison of normal children and children with early childhood autism. The ordinate shows mean coherence. For further details see caption to Fig. 1.

in our study was consistent with these reports. This rhythm is a sensitive indicator of the development of pathological processes in the brain [2]. In addition, the characteristics of theta-rhythm maturation have prognostic value in relation to the development of autistic abnormalities [21]. In healthy subjects, the topographic features of functional connections in the theta rhythm reflect the degree of cortical activation: the more marked the theta rhythm in the anterior leads, the greater the activation of neural networks [24] and the maintenance of voluntary nonspecific attention [10]. At age 5–7 years, the age of the children in our study, the theta rhythm is the most sensitive indicator of changes in functional state on cognitive loading [16]. This raises the question of why the children with early childhood autism studied here do not show significant changes in measures of the theta rhythm – spectral power and coherence – despite successful performance of the task. Adults with schizophrenia with positive symptomatology are known to show hypofrontality – an increase in power of the slow (delta and theta) rhythms in the anterior areas, providing evidence of the involvement of diencephalic limbic structures [13]. A decrease (not increase) in baseline theta-rhythm power in autistic children, as compared with normal children, may be evidence supporting greater similarity between this condition and schizophrenia with dominance of negative symptomatology. This is also indicated by the increase in gamma-rhythm power compared with normal. The great similarity between these two disorders may also be indicated by the common tendency to decreased power in the gamma range seen in patients with ECA and in patients with schizophrenia with negative symptomatology on cognitive loading. The decrease in theta-rhythm reactivity in response to cognitive loading as compared with normal children seen by ourselves has also been described for the fast rhythms in both early childhood autism [7, 8] and in schizophrenia with negative symptomatology [9, 13–15, 26].

Of interest was the reciprocal relationship between the low- and high-frequency rhythms seen in our studies. Thus, in normal children, counting displaced the focus of theta activity into the right hemisphere and the focus of gamma activity into the left hemisphere. The spectral power of the low-frequency theta rhythm in normal children decreased during cognitive loading from the baseline level, while spectral power in the high-frequency gamma rhythm increased. While theta-rhythm spectral power in autistic children was lower than in normal children in baseline conditions, gamma-rhythm spectral power was greater. These reciprocal interactions also applied to changes in the coherence of the two rhythms studied here. It is known that different frequencies may be associated with different cognitive processes. Thus, the gamma rhythm is associated with information processing in cortical neural networks and the theta rhythm with the formation of traces on memorization, while gamma-theta interfrequency interactions are linked with processes forming short-term memory [22]. Alpha-theta [27] and theta-gamma [23] interfrequency interactions contribute to integrative processes during performance of cognitive tasks. Thus, the reciprocal relationships between the theta and gamma rhythms in normal children and children with childhood autism are of particular interest. These may reflect the functioning of mirror neuron systems, which are associated not only with imitation of movements or imagination of movements, but also with performance of a wide spectrum of cognitive functions and suffer both in autism [20] and schizophrenia [18]. The fact that children of the control group showed increases in theta rhythm power in the right hemisphere leads and gamma rhythm power in the left hemisphere during activity may be evidence that the task presented elicits some difficulties in normal children and that its performance is emotionally colored. In patients, counting did not shift the focus of theta activity, which may be a manifestation of a smaller influence from activatory structures of the limbic system associated with operative memory and with a lower emotional significance for the task executed.

In severe autistic disorders, increases in the theta rhythm in all areas, with predominance in the parietal and parietal-central areas, reflects dysfunction of the frontal lobes, manifest as decreases in inhibitory control from the prefrontal cortex over other cortical areas and subcortical structures. Increases in theta activity have been described in the central and central-parietal areas at the moment at which the psychotic state is at its most acute, with displacement into the parietal areas as the pathological state becomes less severe [12]. This gives the impression that in the case of studies of high-functional autists we are dealing with a different mechanism, perhaps not break-up of mental activity but a different cerebral organization of activity associated with impairment to the optimum distribution of excitation in the cortical areas, along with a different emotional coloration of this activity.

CONCLUSIONS

1. In early childhood autism in children aged 5–7 years with the ability to perform counting activities, there were lower levels of spectral power and mean coherence in the theta rhythm and higher levels of spectral power and mean coherence in the gamma rhythm in baseline conditions as compared with healthy subjects, which is consistent with the manifestations characteristic of schizophrenia with negative symptomatology.

2. In healthy subjects aged 5–7 years, performance of a cognitive task increased theta-rhythm power in the right hemisphere leads, which may be evidence of the emotional significance of the task performed, and also increased gamma activity power in the left hemisphere. These changes did not occur in patients with early childhood autism.

3. In early childhood autism, successful performance of the cognitive task was supported by different neurophysiological mechanisms from those operating in normal children.

This study was supported by the Russian Humanities Scientific Foundation (Grant No. 110600863a) and the "Basic Sciences – Medicine" Program of the Presidium of the Russian Academy of Sciences.

REFERENCES

1. V. M. Bashina, *Autism in Childhood*, Meditsina, Moscow (1999).
2. N. K. Blagosklonova and L. A. Novikova, *Pediatric Clinical Electroencephalography*, Meditsina, Moscow (1994).
3. S. V. Borisov, A. Ya. Kaplan, N. L. Gorbachevskaya, and I. A. Kozlova, "Analysis of EEG structural synchronicity in adolescents with schizophrenia spectrum disorders," *Fiziol. Cheloveka*, **31**, No. 3, 1–8 (2005).
4. N. L. Gorbachevskaya, *Features of the Formation of the EEG in Healthy Children and Children with Various Types of General (pervasive) Developmental Disorders: Auth. Abstr. Dissert. Doct. Biol. Sci.*, MGU, Moscow (2000).
5. A. P. Kulaichev, *Computerized Electrophysiology*, Izd. MGU, Moscow (2002).
6. A. P. Kulaichev, *Methods and Systems for Complex Data Analysis*, FORUM: INFA-M, Moscow, (2006).
7. E. A. Lushchekina, E. D. Podreznaya, V. S. Lushchekin, et al., "Features of EEG spectral power in children with early childhood autism and their association with the development of the early symptoms of schizophrenia," *Zh. Vyssh. Nerv. Deyat.*, **61**, No. 5, 1–8 (2011).
8. E. A. Lushchekina, E. D. Podreznaya, V. S. Lushchekin, and V. B. Strelets, "Comparative studies of the EEG in health an early childhood autism," *Zh. Vyssh. Nerv. Deyat.*, **60**, No. 5, 526–535 (2010).
9. R. A. Magomedov, Zh. V. Garakh, Yu. V. Orekhov, et al., "The gamma rhythm, positive, negative symptoms, and cognitive dysfunction in schizophrenia," *Zh. Nevropatol. Psikhiat.*, **101**, No. 1, 78–83 (2010).
10. R. I. Machinskaya and A. V. Kurganskii, "Comparative electrophysiological studies of the regulatory components of working memory in adults and children aged 7–8 years. Analysis of the coherence of rhythms," *Fiziol. Cheloveka*, **38**, No. 1, 5–19 (2012).
11. V. Yu. Novototskii-Vlasov, Zh. V. Garakh, and V. P. Kovalev, "A method for suppressing repeating artefacts on multichannel EEG traces," *Fiziol. Cheloveka*, **33**, No. 2, 115–120 (2007).
12. N. V. Simashkova, L. P. Yakupova, and V. M. Bashina, "Clinical and neurophysiological aspects of severe forms of autism in children," *Zh. Nevropatol. Psikhiat.*, **106**, No. 7, 78–83 (2006).
13. V. B. Strelets, "Mapping of brain biopotentials in emotional and cognitive pathologies," *Zh. Vyssh. Nerv. Deyat.*, **47**, No. 2, 226–241 (1997).
14. V. B. Strelets, Zh. V. Garakh, V. Yu. Novototskii-Vlasov, and R. A. Magomedov, "Relationship between power and synchronization of EEG rhythms in health and cognitive pathology," *Zh. Vyssh. Nerv. Deyat.*, **55**, No. 4, 496–504 (2005).
15. V. B. Strelets, V. Yu. Novototskii-Vlasov, Zh. V. Garakh, et al., "Multiparametric combinatorial analysis of EEG rhythms in health and schizophrenia," *Zh. Vyssh. Nerv. Deyat.*, **57**, No. 6, 684–691 (2007).
16. D. A. Farber, "Principles of the structural-functional organization of the brain and the main stages in its formation," in: *Structural-Functional Organization of the Developing Brain*, D. A. Farber (ed.), Nauka, Leningrad (1990), pp. 168–177.
17. G. Buszaky, *Rhythms of the Brain*, Oxford Univ. Press, Oxford (2006).
18. P. G. Enticott, K. E. Hoy, S. E. Herring, et al., "Reduced motor facilitation during action observation in schizophrenia: A mirror neurons deficit?" *Schizophr. Res.*, **102**, 116–121 (2008).
19. T. Lepisto, T. Kujala, R. Vanhala, et al., "The discrimination of and orienting to speech and nonspeech sound in children with autism," *Brain Res.*, **1066**, No. 1–2, 147–157 (2005).
20. J. Martineau, S. Cochin, R. Magne, and C. Barthelemy, "Impaired cortical activation in autistic children: Is the mirror neurons system involved?" *Int. J. Psychophysiol.*, **68**, 35–40 (2008).
21. P. Mundy, "Annotation: The neural basis of social impairments in autism: the role of the dorsal medial-frontal cortex and anterior cingulate system," *J. Child Psychiatry*, **44**, No. 6, 793–809 (2003).
22. G. Rippon, J. Brock, C. Brawn, and J. Boucher, "Disordered connectivity in the autistic brain: Challenges for the 'new psychophysiology,'" *Int. J. Psychophysiol.*, **63**, 164–172 (2007).
23. B. Schack, V. Nath, H. Petsche, et al., "Phase-coupling of theta-gamma EEG rhythms during short-term memory processing," *Int. J. Psychophysiol.*, **44**, 143–163 (2002).
24. R. Scheeringa, M. C. M. Bastiaasen, K. M. Petersson, et al., "Frontal theta EEG activity correlates negatively with the default mode network in resting state," *Int. J. Psychophysiol.*, **67**, 242–251 (2007).
25. T. Stroganova, E. Orekhova, M. Tsetlin, et al., "EEG evidences of aberrant brain functioning in young children with autism," *Int. J. Psychophysiol.*, **69**, 203–204 (2008).
26. G. Tononi and G. M. Edelman, "Consciousness and complexity," *Science*, **282**, 1846–1851 (1998).
27. A. Von Stein and J. Sarnthein, "Different frequencies for different scale of cortical integration: from local gamma to long-range alpha/theta synchronization," *Int. J. Psychophysiol.*, **38**, No. 3, 301–314 (2000).