Correlations between the EEG Spectral Characteristics and the Severity of Autistic Manifestations

DOI: 10.17691/stm2019.11.1.10
Received October 22, 2018

© **A.B. Sorokin,** PhD, Principal Researcher[1]; Senior Researcher, Department of Functional Diagnostics, University Clinic[2]; Affiliated Researcher[3];
O.V. Balandina, Head of the University Center for Psychology and Child Development[2];
S.A. Polevaya, DSc, Head of the Department of Neurophysiology, Central Scientific Research Laboratory[2]; Head of the Department of Psychophysiology[4];
G.A. Mishanov, PhD Student, Department of Psychiatry and Medical Psychology[2]; Psychiatrist, University Center for Psychology and Child Development[2];
L.V. Savchuk, PhD Student, Department of Psychophysiology[4]; Junior Researcher, Department of Neurophysiology, Central Scientific Research Laboratory[2];
V.V. Borzikov, Junior Researcher, Department of Functional Diagnostics, University Clinic[2];
V.V. Dvoryaninova, Assistant, Department of Psychiatry and Medical Psychology[2]; Junior Researcher, Department of Functional Diagnostics, University Clinic[2];
A.N. Belova, MD, DSc, Professor, Head of the Department of Functional Diagnostics, University Clinic[2]; Head of the Department of Medical Rehabilitation[2]

[1]Federal Resource Center for Organizing Comprehensive Support for Children with Autism Spectrum Disorders, Moscow State University of Psychology and Education, 29 Sretenka St., Moscow, 127051, Russia;
[2]Privolzhsky Research Medical University, 10/1 Minin and Pozharsky Square, Nizhny Novgorod, 603005, Russia;
[3]Haskins Laboratories, 300 George St. #900, New Haven, CT 06511, USA;
[4]National Research Lobachevsky State University of Nizhny Novgorod, 23 Prospekt Gagarina, Nizhny Novgorod, 603950, Russia

Analyzing the brain bioelectrical activity by EEG at rest is a simple and accessible method of research in children. Spectral EEG analysis can identify areas where certain types of activity, that reflect the excitation and inhibition balance, are predominant. Research is complicated by the lack of biological tests for the diagnosis of autism, the illness is diagnosed by clinical characteristics only. Thus, the gold standard of diagnostics is ADOS-2, a technique that assesses the severity of social communication deficits and stereotypical behavior in a child by observing his/her play and interaction.

The aim of the study was to assess the EEG spectral characteristics for their correlation with the ADOS-2 score that reflects the severity of autistic manifestations.

Materials and Methods. Eighteen children with a confirmed diagnosis of "childhood autism" were examined using ADOS-2. To assess the severity of autism manifestations, we used the comparative ADOS-2 score. Resting state EEG was collected for all subjects with subsequent calculation of the relative spectral power.

Results. The examined children showed various degrees of autism, and their comparative ADOS-2 score ranged from 4 to 10. A positive correlation of the comparative score with the EEG spectral power at several leads was revealed. The best correlation was found in the beta range of EEG: the higher the beta activity level, the more pronounced the autistic manifestations. The result indicates that the imbalance between excitation and inhibition is gradually involved in the pathogenesis of autism. Therefore, the spectral power value in the beta range can be potentially used as a dynamic indicator of autism when behavioral changes are difficult to assess.

Conclusion. The relative EEG spectral power in the beta range positively correlates with the ADOS-2 comparative score and therefore can serve as a dynamic biomarker of autism.

Key words: autism; ADOS-2; EEG in autism; spectral analysis of EEG.

Introduction

Autism spectrum disorders are among the most common developmental disorders — up to 1 case per 59 people [1]. In the ICD-10 classification [2], this illness incorporates several subtypes such as childhood autism (F84.0), atypical autism (F84.1), and Asperger syndrome (F84.5). In the ICD-11 [3] various subtypes of autism

Corresponding author: Oksana V. Balandina, e-mail: neurorazvitie@yandex.ru

will be unified into one diagnostic category — autism spectrum disorder (6A02), following recent diagnostic trend.

Autism is heterogeneous in its manifestations, yet all patients with autism have social interaction and communication deficits as well as stereotypical and repetitive behaviors beginning at an early age [4]. In 10–30% of patients, autism is caused by the known genetic defect [5], along with that, many pathogenetic aspects of the genetic and the idiopathic forms require further study.

There is no biological test available to diagnose autism; the diagnosis is based on behavioral manifestations and information from parents. To increase the objectivity of the diagnostic examination and the interpretation of anamnestic data, standardized methods for diagnosing autism have been developed. They are available to psychiatrists and other medical, psychological, and education professionals. The gold standard for diagnosing autism is the "Autism Diagnostic Interview-Revised" (ADI-R) [6] and the "Autism Diagnostic Observation Schedule" (ADOS-2) [7]. Those protocols represent guidelines for interviewing parents and describing the behavior of the examined child. The ADOS-2 includes 10–15 tasks, in which the subject may or may not show social initiatives and reactions; those are assessed by the interviewer according to certain criteria. The resulting scores in the categories "Speech and Communication", "Mutual Social Interaction", "Play and Creativity", "Stereotyped and Repeated Behaviors", and "Other Behaviors" are processed by an algorithm and then compared to the threshold values for diagnosing "autism" or "autism spectrum". For toddlers, instead of the diagnostic groups, the range of concern is determined to report on the possibility of autism spectrum disorder [8]. In addition to the ADOS-2 diagnostic category, the severity of autistic manifestations is determined using a 10-point scale. This metric allows for assessing the degree of manifestations in a particular subject compared to other children with autism of the same age and level of expressive speech. Unlike the "raw" ADOS-2 score, this comparative score is calibrated and thus serves a more stable indicator of the individual characteristics [9]. Depending on the value of the comparative score, the severity of autistic manifestations is defined as "high", "moderate", "low", and "minimal (no symptoms)".

In parallel with improving the diagnostic tools based on the behavioral manifestations, the search for autism biomarkers continues. One of the most promising approaches is the resting-state electroencephalogram (EEG) [10, 11]. It allows the brain potentials integrating the activity of neuron populations to be recorded with a high temporal resolution. The subject is required to cooperate by closing his/her eyes for a few minutes. The recording is then visually analyzed to identify pathological patterns, including epileptiform activity, which is of particular diagnostic significance due to a high comorbidity of autism and epilepsy [12].

With the spectral analysis of EEG one can identify areas with a predominant activity, which allows interpretation in terms of the excitation and inhibition balance [13]. The spectral power is believed to be the main spectral characteristic of the EEG; it is measured either in the range of individual narrow (1 Hz) bands or at the standard frequency bands: delta (up to 4 Hz); theta (4–7 Hz); alpha (7–13 Hz); beta (13–30 Hz), often divided into beta-1 (13–20 Hz) and beta-2 subranges (20–30 Hz); gamma (above 30 Hz). These spectral power values can be compared between groups of patients, and also subjected to correlation analysis versus other parameters, including the behavioral characteristics.

There are few studies of the EEG spectra in patients with autism, and their results sometimes contradict each other [14]. For example, there are reports on both an increase [15, 16] and a decrease [17] in the theta-activity in autists as compared to their typically developing peers. The most commonly documented change is an increased level of the "fast" activities — beta and gamma [15, 18, 19]. It might be caused by the GABA-dependent shift in the balance between excitation and inhibition towards excitation in the central nervous system [20].

The aim of the study was to identify correlations between the comparative ADOS-2 score (reflecting the severity of cognitive and affective manifestations of autism), and EEG spectral characteristics.

Materials and Methods

The study included 18 children with confirmed "childhood autism" (ICD-10 code F84.0), including 12 boys and 6 girls. The average age of participants was 5.3±1.5 years. The study was conducted in accordance with the Helsinki Declaration (2013) and approved by the Ethics Committee of the Privolzhsky Research Medical University. Informed consent was obtained from parents of the examined children.

Fifteen patients had speech problems: they could produce isolated words only or lacked the ability of verbal communication. These children were examined using the ADOS-2 Module 1. Three children had phrased speech and were therefore examined using Module 2. The severity of autistic manifestations was assessed using the comparative ADOS-2 score that was calculated from the "raw" score corrected by age and expressive speech skills.

EEG recording was performed using an EEG-21/26 "Encephalan-131-03" EEG-analyzer (Medicom MTD, Russia). The recording was conducted using 19 electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2), arranged according to the standard 10–20 scheme. The sampling rate was 250 Hz. Filtration of the original signal was performed with the high frequency cut-off value of 0.5 Hz, the low-frequency filter — 70 Hz, the rejector frequency filter — 50 Hz. The impedance values did not exceed

10 kΩ. Artifact-free recording sections were subjected to the fast Fourier transform, the results of which were presented as the spectral power values. To minimize individual variations within the group, the signal was further processed to result in relative spectral power values in the standard frequency bands — delta, theta, alpha, and beta, as well as the narrow bands with a step of 1 Hz. Correlation analysis between the spectral power values and the comparative ADOS-2 scores was performed using the Spearman criterion. The correlation coefficient values above 0.413 ($p<0.05$) were considered significant. The results are presented in correlation coefficient values for various EEG leads in either narrow or standard frequency ranges. Statistical processing and mapping were performed using the Neuro-KM package.

Table 1

The ADOS-2 scores of the examined children

No.	Diagnostic category according to ADOS-2	Comparative score
1	Autism	7
2	Autism	8
3	Autism	8
4	Autism	9
5	Autism	10
6	Autism	6
7	Autism	7
8	Autism	6
9	Autism	5
10	Autism	8
11	Autism spectrum	4
12	Autism	7
13	Autism spectrum	6
14	Autism	7
15	Autism	7
16	Autism	6
17	Autism	10
18	Autism	6

Results and Discussion

Following the ADOS-2 testing, 16 children belonged to the diagnostic category “autism”, and 2 — diagnostic category “autism spectrum”. The comparative scores ranged from 4 to 10 corresponding to moderate or high level of autistic manifestations. They are presented in Table 1.

Correlation analysis of the autistic manifestations and the EEG spectral parameters produced the following results. The ADOS-2 comparative score positively correlates with the spectral power in the beta-1 frequency band, for the F3, Fz, F8, T4, and P3 leads ($R=0.425$, 0.421, 0.442, 0.420, 0.445, respectively; all $p<0.05$), in the beta-2 frequency band, for the Pz lead ($R=0.436$; $p<0.05$), and also in the beta-1 frequency band (with a borderline significance), for the Pz zone ($R=0.412$; $p=0.05$). The results of the EEG mapping are presented in Figures 1 and 2.

In the narrow 1 Hz frequency bands, significant Spearman correlations were found in frequency bands of 2–3 Hz (F8), 5–6 Hz (F8, Fp2), 6–7 Hz (F8), 12–13 Hz (F8, Pz, P4, T6), 14–15 Hz (F3, Fz, F8, T4), 15–16 Hz (Fz, F8, T4), 17–18 Hz (F3, Fz, Fp1), 18–19 Hz (F7, P3, P4, O2), 19–20 Hz (F7, Fz, F8, P3, Pz), 23–24 Hz (P3, Pz), 27–28 Hz (Pz), 28–29 Hz (P3, Pz), and 29–30 Hz (Fz, P3, Pz). All correlations were positive; the correlation coefficient values are presented in Table 2.

In our study on both the standard width bands and the 1 Hz-bands, major correlations were found in the beta EEG range. Interpretation of correlations in the delta and theta ranges is complicated because they are rather scarce and appear only in the outer frontal and temporal zones that are most vulnerable to motor artifacts.

The correlations between the clinical manifestations of autism and the most consistent changes in EEG spectral

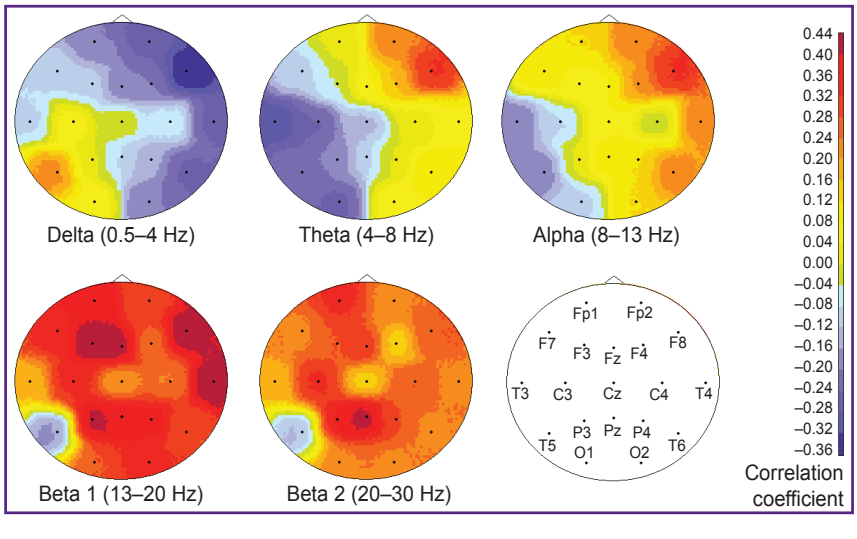

Figure 1. Correlation between the relative spectral power (% of the entire range) and the ADOS-2 comparative score for leads Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2

The Spearman coefficient values significantly differ from zero: $R>0.413$; $R<-0.413$ ($p<0.05$)

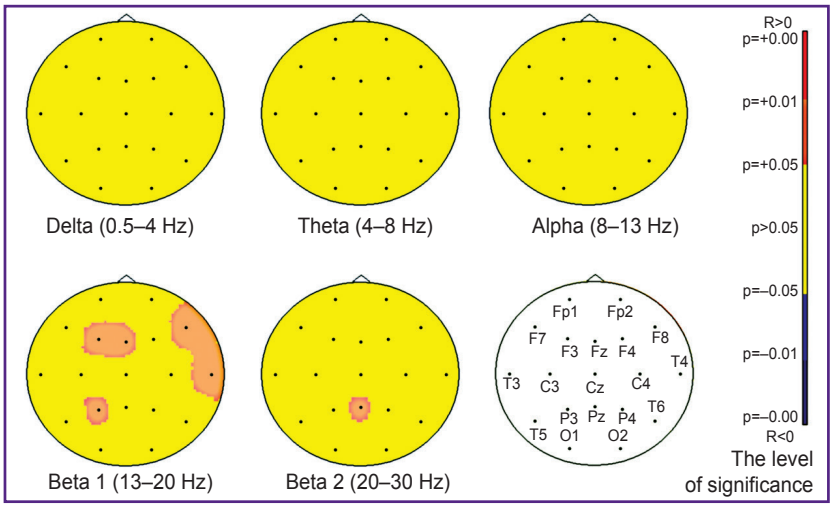

Figure 2. Correlation between the relative spectral power (% of the entire range) and the ADOS-2 comparative score
Spearman's correlation: the positive p values pertain to correlations when R>0; and the negative p values — to correlations when R<0 at leads Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2

Table 2

The Spearman coefficient of correlation between the relative EEG spectral power and the comparative ADOS-2 score at a significance level of p<0.05

Frequency band (Hz)	Lead	R
2–3	F8	0.46
5–6	F8	0.44
5–6	Fp2	0.46
6–7	F8	0.43
12–13	F8	0.45
12–13	Pz	0.43
12–13	P4	0.5
12–13	T6	0.42
14–15	F3	0.44
14–15	Fz	0.43
14–15	F8	0.42
14–15	T4	0.42
15–16	Fz	0.45
15–16	F8	0.47
15–16	T4	0.49
17–18	F3	0.44
17–18	Fz	0.46
17–18	Fp1	0.42
18–19	F7	0.43
18–19	P3	0.42
18–19	P4	0.51
18–19	O2	0.42
19–20	F7	0.44
19–20	Fz	0.42
19–20	F8	0.46
19–20	P3	0.55
19–20	Pz	0.46
23–24	P3	0.45
23–24	Pz	0.43
27–28	Pz	0.45
28–29	P3	0.42
28–29	Pz	0.44
29–30	Fz	0.48
29–30	P3	0.43
29–30	Pz	0.57

characteristics [19, 20], indirectly support the validity of both diagnostic tools. These neurophysiological and behavioral results suggest that the higher the EEG beta activity, the more pronounced the autistic manifestations. This indicates a gradual involvement of the imbalance between excitation and inhibition in the pathogenesis of autism and provides the rationale to using the EEG spectral power in the beta range as an additional diagnostic tool in situations where the behavioral changes are difficult to assess.

Conclusion

In this study, for the first time, a correlation between the severity of autistic manifestations (the comparative ADOS-2 score) and EEG spectral characteristics has been demonstrated. The relative spectral power in the beta range positively correlates with the ADOS-2 comparative score, which supports the concept of increased excitation in the CNS in patients with autism.

Research funding. The study was supported by the "Identification of rehabilitation predictors in motor and cognitive impairments in children with disabilities (cerebral palsy, retarded static-motor and psychological development, etc.)" program.

Conflicts of interest. A.S. received compensation for translating and editing ADOS-2 as well as for teaching professional development courses.

References

1. Baio J., Wiggins L., Christensen D.L., Maenner M.J., Daniels J., Warren Z., Kurzius-Spencer M., Zahorodny W., Robinson Rosenberg C., White T., Durkin M.S., Imm P., Nikolaou L., Yeargin-Allsopp M., Lee L.C., Harrington R., Lopez M., Fitzgerald R.T., Hewitt A., Pettygrove S., Constantino J.N., Vehorn A., Shenouda J., Hall-Lande J., Van Naarden Braun K., Dowling N.F. Prevalence of autism spectrum disorder among children aged 8 years — autism and developmental disabilities monitoring network, 11 sites, United

States, 2014. *MMWR Surveill Summ* 2018; 67(6): 1–23, https://doi.org/10.15585/mmwr.ss6706a1.

2. World Health Organization. *Mezhdunarodnaya klassifikatsiya bolezney* (10-y peresmotr) [International classification of diseases (10th revision)]. Saint Petersburg: Adis, 1994.

3. *ICD-11: mortality and morbidity statistics*. URL: https://icd.who.int.

4. Lai M.C., Lombardo M.V., Baron-Cohen S. Autism. *Lancet* 2014; 383(9920): 896–910, https://doi.org/10.1016/s0140-6736(13)61539-1.

5. Vorstman J.A.S., Parr J.R., Moreno-De-Luca D., Anney R.J.L., Nurnberger J.I. Jr., Hallmayer J.F. Autism genetics: opportunities and challenges for clinicaltranslation. Autism genetics: opportunities and challenges for clinical translation. *Nat Rev Genet* 2017; 18(6): 362–376, https://doi.org/10.1038/nrg.2017.4.

6. Rutter M., Le Couteur A., Lord C. *ADI-R. Intervyu dlya diagnostiki autizma* [Autism diagnostic interview-revised]. Pod. red. Sorokina A. [Sorokin A. (editor)]. Western Psychological Services; Giunti O.S.; 2014.

7. Lord C., Rutter M., DiLavore P., Risi S., Gotham K., Bishop S.L., Luyster R.D., Guthrie W. *ADOS-2. Plan diagnosticheskogo obsledovaniya pri autizme* [ADOS-2. Autism diagnostic observation schedule]. Western Psychological Services; Giunti O.S.; 2016.

8. Sorokin A.B., Davydova E.Y. Autism diagnostic evaluation schedule (ADOS-2) for evaluation of behavior and communication in toddlers with concern of autism spectrum disorder. *Autizm i narusheniya razvitiya* 2017; 15(2): 38–44, https://doi.org/10.17759/autdd.2017150204.

9. Gotham K., Pickles A., Lord C. Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *J Autism Dev Disord* 2009; 39(5): 693–705, https://doi.org/10.1007/s10803-008-0674-3.

10. Heunis T.M., Aldrich C., de Vries P.J. Recent advances in resting-state electroencephalography biomarkers for autism spectrum disorder — a review of methodological and clinical challenges. *Pediatr Neurol* 2016; 61: 28–37, https://doi.org/10.1016/j.pediatrneurol.2016.03.010.

11. Yasuhara A. Correlation between EEG abnormalities and symptoms of autism spectrum disorder (ASD). *Brain Dev* 2010; 32(10): 791–798, https://doi.org/10.1016/j.braindev.2010.08.010.

12. Buckley A.W., Holmes G.L. Epilepsy and autism. *Cold Spring Harb Perspect Med* 2016; 6(4): a022749, https://doi.org/10.1101/cshperspect.a022749.

13. *Brain electrical activity mapping for diagnosing psychiatric disorders: a review of the clinical evidence. Rapid response report: summary with critical appraisal.* Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2014.

14. Devitt N.M., Gallagher L., Reilly R.B. Autism spectrum disorder (ASD) and fragile X syndrome (FXS): two overlapping disorders reviewed through electroencephalography — what can be interpreted from the available information? *Brain Sci* 2015; 5(2): 92–117, https://doi.org/10.3390/brainsci5020092.

15. Coben R., Clarke A.R., Hudspeth W., Barry R.J. EEG power and coherence in autistic spectrum disorder. *Clin Neurophysiol* 2008; 119(5): 1002–1009, https://doi.org/10.1016/j.clinph.2008.01.013.

16. Pop-Jordanova N., Zorcec T., Demerdzieva A., Gucev Z. QEEG characteristics and spectrum weighted frequency for children diagnosed as autistic spectrum disorder. *Nonlinear Biomed Phys* 2010; 4(1): 4, https://doi.org/10.1186/1753-4631-4-4.

17. Shephard E., Tye C., Ashwood K.L., Azadi B., Asherson P., Bolton P.F., McLoughlin G. Resting-state neurophysiological activity patterns in young people with ASD, ADHD, and ASD + ADHD. *J Autism Dev Disord* 2018; 48(1): 110–122, https://doi.org/10.1007/s10803-017-3300-4.

18. van Diessen E., Senders J., Jansen F.E., Boersma M., Bruining H. Increased power of resting-state gamma oscillations in autism spectrum disorder detected by routine electroencephalography. *Eur Arch Psychiatry Clin Neurosci* 2015; 265(6): 537–540, https://doi.org/10.1007/s00406-014-0527-3.

19. Gurau O., Bosl W.J., Newton C.R. How useful is electroencephalography in the diagnosis of autism spectrum disorders and the delineation of subtypes: a systematic review. *Front Psychiatry* 2017; 8: 121, https://doi.org/10.3389/fpsyt.2017.00121.

20. Wang J., Barstein J., Ethridge L.E., Mosconi M.W., Takarae Y., Sweeney J.A. Resting state EEG abnormalities in autism spectrum disorders. *J Neurodev Disord* 2013; 5(1): 24, https://doi.org/10.1186/1866-1955-5-24.