Modern Technologies in Studying the Mechanisms, Diagnostics, and Treatment of Autism Spectrum Disorders (Review)

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Autism spectrum disorders (ASD) are among the most common and intractable neurological diseases characterized by high heterogeneity and requiring a person-oriented approach to diagnostics and treatment. The purpose of this review is to summarize the literature data of the last 5 years on the contribution of modern technologies to the knowledge of mechanisms, diagnostics, and treatment of ASD. Particular attention is paid to the possibilities of non-drug treatment of ASD with the help of neurointerface technologies, including the brain–computer interface and neurofeedback technologies. The advantages of the musical neurointerface elaborated by the authors with complex feedback from brain and heart biopotentials, providing the possibility of personalized treatment of ASD, are grounded.

Key words: autism spectrum disorders; ASD; brain–computer interface; neurofeedback technology; personalized ASD treatment.

Introduction

Autism (from Latin *autos* — “self“, autism — immersion in oneself) is a severe, in many cases disabling, disease of early childhood which is characterized by a severe deficit in communication, social interaction, and speech, by the presence of limited repetitive and stereotyped patterns of behavior and interests, often accompanied by intellectual underdevelopment [1]. Until the middle of the XX century, a disease such as autism did not exist — children and adults with autism were most often diagnosed with schizophrenia. For the first time autism as a disease was described in 1942 by American clinician Leo Kanner, a little later in 1943, a similar disorder of children was described by Austrian doctor Hans Asperger, and in 1947 — by Russian neurologist Samuel Mnukhin [2]. Later, due to the extreme heterogeneity of the states, the multiplicity of etiologies, subtypes, and dynamics of the development of the disease, it began to be referred to the group of autism spectrum disorders (ASD) [3].

The problem of autism spectrum disorders is among the most complex and actual due to high prevalence of this pathology — 1–2% in the infant population [4, 5]. The exponential growth of research on this problem began to occur at the end of the last century when there was a kind of “epidemic” of diagnoses of autism [6, 7]. Until now, it has not been finally established whether the high prevalence of autistic disorders is a consequence of the actual increase in morbidity or is associated with overdiagnosis and dilution of the diagnostic boundaries of autism by the classifications used in modern psychiatric practice [8, 9]. The high relevance of the problem is evidenced by the fact that in 2014 the 67th World Health Assembly adopted a resolution on “Comprehensive and Coordinated Efforts for the Management of Autism Spectrum Disorders”, supported by 60 countries.

In recent years, there has been an increase in interest to the problem of autism spectrum disorders, and the number of publications on this topic has doubled over the past five years. In the literature, new data on the nature, mechanisms of occurrence, diagnosis, and treatment of ASD have appeared. The task of the presented review is a detailed consideration of these issues, as well as the contribution of modern technologies to solving the problems of the ASD. Particular attention is paid to the possibilities of ASD treatment with the help of neurointerface technologies. The advantages of the musical neurointerface developed by the authors are grounded.

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Modern views on the nature and mechanisms of autism spectrum disorders

By now, it is generally accepted that ASD are a heterogeneous set of developmental disorders that are neurological in nature, which appear in early childhood and are characterized by a reduced level or lack of age-appropriate social contacts with other people and unusually limited, stereotyped types of behavior, interests, and activity [10]. It is also known that ASD affect more men than women [11], and are often accompanied by comorbid disorders — mental retardation [12], delayed speech development [13], epilepsy [14], depression [15], anxiety [16], attention impairments [17–19].

Children with ASD have sensory hypersensitivity, fragmented and distorted perception, difficulties in processing of sensations [20]. They have much more frequent than normal, phenomena of synaesthesia, or perception, in which the stimulation of one sensory channel causes sensations in other senses. Such children see the sounds or smell of color, geometric figures for them have a taste, they feel the skin colors or hear colors, etc. [21]. There is evidence that sensory dysfunction in ASD persists with age in adolescents and adults [22, 23].

Patients with ASD avoid eye contact with others, are extremely discriminating in everyday life, they are characterized by stereotypical movements and motor actions, as well as speech stereotypes associated with the desire to maintain a monotonous state [24]. With the slightest change in the habitual conditions of life, these patients have a sharply negative reaction accompanied by special emotional states — withdrawal into themselves and emotional disruptions [25].

The actual causes of the development of ASD have not been fully revealed, but most researchers believe that these diseases are based on a combination of genetic and epigenetic factors with the environmental factors [26, 27]. Such key processes as neurogenesis, neurite outgrowth, synaptogenesis and synaptic plasticity [28], as well as atypical cortical organization and reduction in the integrity of the gray and white matter of the brain [29], are considered as key pathophysiological mechanisms of the ASD.

High technology in the diagnosis of autism spectrum disorders

The problem of ASD diagnostics is extremely urgent since untimely diagnosis increases the course of the underlying disease and increases the risk of forming comorbid disorders [30]. In recent years, thanks to the introduction of modern technologies in clinical practice, several promising approaches to solving this problem have been formed.

A definite place in the development of promising approaches to the diagnosis of ASD belongs to the methods of quantitative electroencephalography (EEG) [31, 32]. Thus, with the use of the quantitative EEG analysis in the ASD, the disturbances in the interconnectedness of brain regions at rest have been established [33], and the peak frequency of the EEG alpha-rhythm has been proposed as a biomarker of cognitive functions in ASD [34].

The development of increasingly effective approaches to the computer analysis of non-invasively recorded characteristics of patients with ASD has made it possible to demonstrate the diagnostic potential of other bioelectrical parameters, such as the electrocardiogram [35] and heart rate variability [36], a magnetoencephalogram [37], electromyogram [38] and others. Given the difficulties of contact with ASD patients, innovative diagnostic methods based on biochemical analysis of saliva seem to be promising [39–41].

Due to the fact that one of the most characteristic signs of ASD is the avoidance of eye contact with others [42], the development of diagnostic sensory technologies, and primarily eye tracking technologies [43]. Thus, algorithms have been developed for early diagnosis of ASD on the basis of a comparative analysis of eye movements in the presentation of social or abstract scenes to the patient [44]. To identify the features of visual contact in social interactions, a special narrow-chamber camera is proposed instead of the stationary one [45], ASD patients have been examined for mechanisms of reduced attention to the eyes of others [46]. A method has been developed for the computer analysis of facial expressions in social interactions, which makes it possible to identify such a marker of ASD as reduced intensity of facial expression [47].

In recent years, the technology of genetic testing attracts more and more attention of the investigators searching for effective approaches to the diagnosis of ASD [48]. Thus, a technology has been proposed for the determination of mutations in the sequence of genes that can be observed only in patients with ASD, but do not occur normally [49]. In the United States, a national database on autism is created that includes the genomic and neurobiological data of thousands of patients and allows big data technology to be used to locate ASD markers [50]. It is believed that the progress of genetic testing technologies in the near future will open new prospects for treating ASD [51].

Traditional approaches to the treatment of autism spectrum disorders

To date, it is generally accepted that ASD are incurable diseases due to extreme heterogeneity of states, the multiplicity of etiologies, subtypes and developmental trajectories of the disease [52]. At the same time, it is pointed out that the most effective approach to ASD treatment is early assistance to children, providing for the initiation of corrective measures in the course of diagnosis [53]. This can be done by telemedicine examination of patients [54], during which not only the timely diagnosis of ASD but also the medical advice of specialists can be given [55].

At the moment there is no specific drug therapy for ASD, and drugs can only reduce the comorbid symptoms [56]. Therefore, the methods of cognitive-behavioral therapy aimed at the formation of socially acceptable behavior, structured skills training, as well as analysis and training in verbal behavior have received the most widespread applications in the treatment of ASD [57–59].

In evaluating the possibilities of complementary and alternative therapy in the treatment of ASD, the most promising are considered such interventions, as musical therapy [60–62], sensory-integration therapy, or sensory enrichment of the environment [63], acupuncture [64] and massage [65]. A technology is proposed to enhance physical activity in children with ASD, aimed at developing increased physiological responses to dynamic movements by continuously measuring energy expenditure and heart rate during specially organized training [66].

Gameplay is an important means of correcting the emotional development of children with autism [67]. During the game, the ASD children develop skills for active interaction with the environment, develop their moral, intellectual, emotional-volitional qualities, develop their personality, expand the circle of communication, form the functions of adaptation and socialization [68]. Therefore, the inclusion of gaming components in therapeutic procedures in ASD is considered extremely useful in reducing the symptoms associated with the disease [69]. Games are effectively used to improve behavior, cognitive processes and the regulation of emotions in ASD children in neurointerface technologies [70], discussed in detail in the next section.

Neurointerfaces in the treatment of autism spectrum disorders

In recent years, neurointerface technologies, including the brain–computer interface and neurofeedback, have become a healing tool for many psychic [71, 72] and neurological [73–75] disorders, restoration and improvement of nervous, cognitive and behavioral human functions [76–79].

Brain–computer interfaces are software and hardware systems for recognizing and decoding patterns of brain bioelectric activity, available for voluntary control by the user [80, 81]. In neurofeedback technologies, various biophysical characteristics of the human body are transformed into informative feedback signals for learning the skill of arbitrary regulation of various functions [82, 83].

A common feature of these technologies is their extreme personalization through the use of feedback from the individual bioelectric characteristics of the patient in the organization of therapeutic interventions [84]. This is especially important because due to the high heterogeneity of the ASD the development of personalized approaches to their diagnosis and treatment is considered the most promising direction of research [85]. A number of recent works that successfully apply the technology of neurointerfaces both in diagnosis and in the treatment of ASD confirm this statement.

The most widely the neurointerfaces employing biopotentials of the brain (electroencephalogram) as feedback signals are used [86]. Clinical experience suggests reasonable safety of neurointerfaces to treat a variety of pediatric diseases, including ASD, and demonstrates the efficacy of these medical procedures [87]. For example, using EEG neurofeedback sessions in ASD patients, the marked normalization of behavioral and electrophysiological parameters due to increasing the structural and functional interrelationship of brain regions [88]. Under EEG neurofeedback procedures in ASD patients, the positive changes have been revealed in several characteristics, such as behavior (they become less aggressive and more contact), in indicators of attention, memory and motor skills, as well as in the overall level of daily functioning [89]. EEG neurofeedback is considered to be an effective method of correcting psychophysiological characteristics in patients with ASD [90].

The original neurointerface is recently developed for detection and suppression of anxiety states in ASD [91]. The interface, called “biomusic”, maps physiological signals to music (i.e., electrodermal activity to melody; skin temperature to musical key; heart rate to drum beat; respiration to a “whooshing” embellishment resembling the sound of an exhalation). Listening to these signals helps subjects to make intuitive detection and suppression of unfavorable states.

Analysis of the literature shows that two progressive trends are observed in the development of neurointerface technologies. One of them consists in the development of approaches that involve the use of musical or music-like feedback signals from one’s own bioelectric characteristics, which facilitate the patient’s perception of them and contribute to increasing the effectiveness of therapeutic procedures [92–94]. The second trend is related to the intention to develop multimodal [95] or hybrid [96] neurointerfaces, which use complex multimodal feedback not only from the parameters of the EEG but also from other body systems [97].

In accordance with the described trends, the authors developed a musical neurointerface combining the ultimate personalization of the EEG neurofeedback with the dignity of the unconscious perception of stimulation that is characteristic for musical therapy [98, 99]. It is based on musical or music-like signals, which are organized in strict accordance with the current values of the biopotentials of the patient’s brain. A distinctive feature of the developed neurointerface, which enhances the personalization of medical procedures, is the use of musical feedback not from excessively broadband traditional EEG rhythms (theta, alpha, beta, etc.), but from the characteristic and significant for the individual narrow-frequency EEG oscillators detected in real time on the basis of a specially developed dynamic approach [100].

The main advantage of the developed musical neurointerface is the possibility of its application for the correction of unfavorable functional states in conditions that do not require the conscious efforts of the subjects. This is especially important in the condition of treatment sessions with children and patients who are characterized by altered mental states or ineffective drug therapy. Therefore, this technology was successfully tested to eliminate stress-induced disorders [101] and risks of functional reliability of the specialist [102]. The advantages of using a musical neurointerface for the treatment of attention deficit hyperactivity disorder [103] and epilepsy [104] are grounded.

In the treatment of ASD, the combined neurointerfaces focusing on the interaction of the brain, body, and behavior of the patient are considered to be particularly effective [105]. Recently, the authors developed and tested in a model experiment a variant of the musical neurointerface [106], in which audio-visual stimuli formed on the basis of the EEG of the subject are supplemented by rhythmic beeps simulating the rhythm of his heartbeats. The data obtained suggest that complex feedback using control signals from the biopotentials of the brain and heart of the patient can be effectively used in the treatment of ASD.

Conclusions

The data reviewed show that in recent years a significant progress has been made in understanding the nature and mechanisms of ASD, as well as in the diagnosis and treatment of these diseases. The most significant results were obtained in the works using modern high technologies, such as quantitative electroencephalography, eye tracking, genetic testing, etc.

An important place in the arsenal of therapeutic means for ASD treatment is beginning to be occupied by the technology of neurointerfaces using feedback from the individual bioelectric characteristics of the patient and thereby providing personalized healing effects. It can be expected that the development of these technologies and their introduction into clinical practice will lead in the nearest future to the development of effective tools for the diagnosis and treatment of ASD.

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