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AUTISM

is not a simple behavioral disorder, but a lifelong CHALLENGE

prof. MUDr. **Daniela Ostatníková**, PhD.
Comenius University Bratislava – Faculty of Medicine

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Content

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Graphic design: Dušan Ščepka.
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prof. MUDr. **Daniela Ostatníková**, PhD.

Was graduated at the Faculty of Medicine – Comenius University in Bratislava, and she completed her postgraduate studies at the same faculty where she is currently a Professor of normal and pathological physiology. She is the guarantor of the postgraduate study program Medical Neurosciences. She established a scientific school which deals with the effects of sexual steroids on cognitive functions and the hormone participance within autism etiology. She has completed several residencies at foreign universities, thanks to the Fulbright Foundation study stay at the University of Michigan (2004) and thanks to Templeton fellowship study stay at the University of Iowa (2008). From 2014 to 2018, she served as a visiting professor at Nova Southeastern University, Florida. Many PhD candidates researching on autism were participants of their studying stays within Mailman Segal Center for Human Development, which is an integral part of that university. She initiated the cooperation with prof. Baron-Cohen at the Autism Research Center at the University of Cambridge, developed by her students. She is the founder of the Academic Research Centre for Autism at the Comenius University Faculty of Medicine.

Abstract

Autism is a neurodevelopmental disorder that is believed to have been the result of several etiological factors affecting the development of the central nervous system in critical periods of life. The consequences are disorders of sensory perception, disruption of social interaction with abnormalities in social communication, along with stereotypical, repetitive behavior and limited interests. Autism represents the whole spectrum of disorders – that is why we are talking about autism spectrum disorders.

It can be said that each individual with autism is different. Heterogeneity is manifested in different severity of the above-mentioned so-called core symptoms of autism, however, there are also varying degrees of adaptability, intellectual capacity, language skills, and associated psychiatric and other concomitant illnesses. The pharmacological treatment of the core symptoms of autism is unknown. Although we do not yet know a cure for autism, behavioral interventions are available to improve the quality of life of disabled persons. Understanding autism merely as a behavioral disorder is very superficial; it is a neurodevelopmental disorder that affects all areas of central nervous system development and its functions with projection into all areas of the life of an individual with autism. If we understand and accept all the limitations that people with autism live with, if we accept them in society, then we can also help them realize their potential to the extent that their limitations allow them.

Keywords: autism spectrum disorders, gene-environment interaction, autism biomarkers, applied behavior analysis.

Abstrakt

Autizmus je neurovývinová porucha, ktorá je vysoko pravdepodobne výsledkom viacerých etiologických faktorov postihujúcich vývin centrálneho nervového systému v kritických obdobiach života. Dôsledkami sú poruchy zmyslového vnímania, narušenie sociálnej interakcie s abnormalitami v sociálnej komunikácii, spolu so stereotypným, repetitívnym správaním a obmedzenými záujmami. Autizmus predstavuje celé spektrum porúch – preto hovoríme o poruchách autistického spektra.

Možno povedať, že každý jedinec s autizmom je iný. Heterogenita sa prejavuje v rôznej závažnosti vyššie zmienených, tzv. jadrových príznakov autizmu, je však prítomná aj rôzna miera adaptability, intelektovej kapacity, jazykových schopností a pridružených psychiatrických a iných sprievodných ochorení. Liečba jadrových príznakov autizmu nie je známa. Aj keď zatiaľ nepoznáme liek na autizmus, je dostupná symptomatická liečba zlepšujúca kvalitu života postihnutých osôb. Chápanie autizmu len ako poruchy správania je veľmi povrchné; je to neurovývinová porucha, ktorá sa týka všetkých oblastí centrálneho nervového systému a jeho funkcií s projekciou do všetkých oblastí života jedinca s autizmom. Ak pochopíme a prijmeme všetky obmedzenia, s ktorými ľudia s autizmom žijú, ak ich budeme v spoločnosti akceptovať, potom im môžeme aj pomôcť uplatniť ich potenciál v rozsahu, ktorý im ich obmedzenia umožnia.

Kľúčové slová: poruchy autistického spektra, interakcia génov a prostredia, biomarkery autizmu, aplikovaná behaviorálna analýza.

What the autism is?

Autism is a lifelong disorder, which is penetrating into all central nervous system components and parts and it is limiting an individual's functionality in his/her daily life. It is being created as a result of a disorder of growth and interconnections of neurons and causes permanent damages related to social interaction area and communication as well, while there appear limited stereotype patterns of interests, or activities. There are also observed increased or decreased reactions to sensory stimuli, or presence of unusual interests related to environment sensory aspects[1]. Despite that the disorder is observed in an individual's childhood, its full range might be seen later, when the environmental demands exceed his/her limited possibilities and capabilities. The people who are suffering from autism have developed core symptoms, however there might be a wide spectrum related to weakening intellectual and linguistic capabilities as well, which, in the final picture, causes very diverse manifestations of the disorder in each of them and creates a unique phenotype in each individual. Therefore, the following definition might be postulated: "How many personalities befallen by autism exist, so many autism types can be observed". In the case, there are accompanying illnesses, the basic autism symptoms seem to be more complicated.

The prevalence of autism spectrum disorders (ASD) indicates an increasing trend round the globe. In Europe, there is one percent of men and women suffering from autism. The reasons of increasing trend are not explained in a full range, however the facts concerned with diagnostic criteria development, overall screening and an accessibility of standardized diagnostic tools seem to be very significant contribution as well. Nevertheless, adults with autism are still being undiagnosed. Growth of scientific works, which deal with autism is increasing and indicates an exponential trend (see also Table 1).

Table 1 A number of scientific works concerned with autism is growing very rapidly

Time period	Number of scientific works
1961 – 1965	122
1966 – 1970	329
1971 – 1975	648
1976 – 1980	765
1981 – 1985	835
1986 – 1990	1 251
1991 – 1995	1 668
1996 – 2000	2 752
2001 – 2005	5 759
2006 – 2010	12 120
2011 – 2015	23 299
2016 – 2020	34 341

Source: The Scopus database, articles related to autism password within article title, abstract or keywords.

1 For example, the man or woman is being fascinated by rotation of washing machine trommel or is suffering by need to smell things, etc.

The Academic Research Center for Autism

The Academic Research Center for Autism (ARCA), being an integral part of Faculty of Medicine, Comenius University in Bratislava established in 2013, created a basis for gaining of biological samples from those children who are suffering from autism, what enabled providing investigations related to autism etiology. The main goal of the centre is to assure integration of research activities aimed to ASD in the Slovak Republic into a co-operating network, when implementing diagnostic and therapeutic protocols with respect to evidence- based medicine. However, ARCA task is to increase autism awareness, to provide education of experts and laypeople and to co-ordinate interaction with patients, their families and co-operating institutions as well. An interdisciplinary co-operation seems to be a unique possible way, when healing that illness by which are befallen the patients and their families too.

The solutions and results related to ARCA projects enabled implementing modern standard screening and diagnostic methods applied to objective diagnosis determination concerned with autism spectrum disorders. Thanks to ARCA activities appropriate recommendations have been developed, which enabled implementing unified access to ASD diagnostic in the Slovak Republic. The standard screening, diagnostics, and treatment together with adequate autism management procedures were approved and validated on July 1, 2021 by the Ministry of Health of the Slovak republic (**https://www.standardnepostupy.sk/nove-standardy/**.)

Fig. 1 The Academic Research Center for Autism

How the autism might be indicated?

Autism spectrum disorders are characterized by the presence of abnormalities in the quality of social interaction and communication; and the presence of narrow, repetitive and stereotypical patterns of behavior. People with autism have problems utilizing social and practical skills as well while the attention and imagination are weak and they lack the ability to evaluate hypothetic situations and to regulate their behavior.

They achieve a very low empathy level, and they are not able to read intensions of other people based on its face-play. However, they do not understand feelings of other people and they are not able of adequate reaction to that feelings, while there is required a behavior flexibility, inference to the future and a social understanding of the entire situation. In the case of personalities suffering from autism these abilities are diminished in a great deal.

When considering repetitive and stereotype behavioral patterns, the children befallen by ASD have a lot of difficulties with adaptation to changes within environment, the specialized interests are observed in their behavior and their stronger concentration to details related to persons and things are indicated as well. Some individuals with autism might show a compulsive inherency to non-functional routines or rituals and that could cause difficulties in changing environments too.

A set of repetitive motoric mannerisms seems to be further evident autism symptom, while a repeated hand flapping, full-body rocking back and forth, or covering ears might be postulated as an example. When the children are playing, they have a lowered imagination or fantasy and, in many cases, a repetitive utilization of toys together with self-stimulating behavior might be observed as well, while some those stereotypes might be closely related to area of sensory stimuli perception too. The children with ASD have an increased or decreased sensitivity to sensory stimulation and an extreme reaction to sound, materials, pain, cold or warmth might be often observed. In many cases rituals related to food taste, scent and visual aspects of food occurs and food selectivity might develop as well.

How autism could be confirmed?

The diagnosis should be preceded by a nationwide screening, with which we search for children with a high probability of autistic disorder in the entire population. The first fears related to that the child is being befallen by autism might be observed at the age of 12 – 24 months. The screening helps us to discover risky children who are undertake to an appropriate diagnostic with the use of adequate methods based on the child observation related to her/his developmental history, while the diagnostics done in time seems to be the key aspect from the child´s development point of view. The sooner is the autism confirmed, the sooner adequate behavioral intervention might get started and that intervention could significantly positively affect further disorder development. The autism symptoms might be mild, however, they could be severe as well and they are being changed with the child life periods, some of them are losing and the other ones appear. However, an individual's ability to function in practical life does not have to depend only on the severity of the symptoms of autism, while his/her intellectual and linguistic abilities play a role of principle importance too. The ASD individuals may or need not have a language disorder and they have a great scale of intellectual capabilities since a high-level intellect up to very important deficits. However, their benefiting depends on occurrence and importance of psychiatric, neurological or other diseases as well.

What about autism reasons?

All actions and steps accompanying everybody's life has its own timing and the same is concerned with our brain thanks to gene expression. The autism is a result of the entire cascade related to central nervous system development disorders, the reasons of which are closely related to genetic, hormonal and immunity factors. The factors, which generate autism phenotype, cause the primary failures related to creation, development, and interconnections of brain cells -neurons within central nervous system. However, the same is concerned with organization of neurons within actual brain areas responsible for perception of a real world, understanding of emotions and social relations together with getting to know the world and utilization of knowledge within real life as well.

Many theories, which did best explain principal autism symptoms have been developed as a result of an intensive research provided at present. Despite that the original theories had been closely related to reasons of autism symptoms, now they are helping to understand a variety of illness manifestations within behavior and cognitive processes, which make problems within real life. Autism seems to be a disease generated by many factors, while more factors are acting simultaneously and most significant aspects are closely related to genetic factors.

Important factors that are intensively studied in relation to the autistic phenotype are hormonal influences and other influences of the body's internal environment, such as immunity or intestinal microbiota. However, there are investigated epigenetic factors as well, while they include different processes affecting expression – it means switching on and switching off the genes without any intervention to sequence of life code – deoxyribonucleic acid. A creation of several proteins might be lowered or removed as a result of gene activity change, while those proteins enable creating enzymes affecting substances conversions or the neurotransmitters, which affect a communication of neurons too.

The environmental effects and interaction of genes with the environment seem to be a subject of the continual research at present as well, while a set of social factors, which cause postponing reproduction to later years increase a risk of further mutations within germline cells of parents and it might be closely related to an increased exposition of environmental risk factor and their interaction with genetic background too. The term mutation means an exchange of characters within the DNA sequence. The above-mentioned exchange might be useful from a long-term point of view and it generates chances for the survival of people within new conditions, because the mutations generate the larger diversity, where the nature might make various selections. On the other hand, when considering a short-term point of view, the genetic information change might result in a brain development damage and therefore the de novo mutations seem to be dangerous and could be associated with autism. The above-mentioned newly created mutations occur in germinative cells only, it means in sperms or ovum, and they become a genetic equipment of descendants, while there is not a concrete gene responsible for autistic phenotype and there also is a complex set of genetic changes within many genes. In general, the autism feature occurrence is common within population and it might be assumed that an accumulation of different gene variants might be a cause of a new phenotype generation which fills in a criterion related to autistic spectrum disorder. This polygenic effect has been confirmed and it means that the relatives of the children within confirmed autistic spectrum disorder have more autistic features in their behavior than the individuals from the common population. It means, the wider autistic phenotype represents a subclinical manifestation of the core symptoms related to autism.

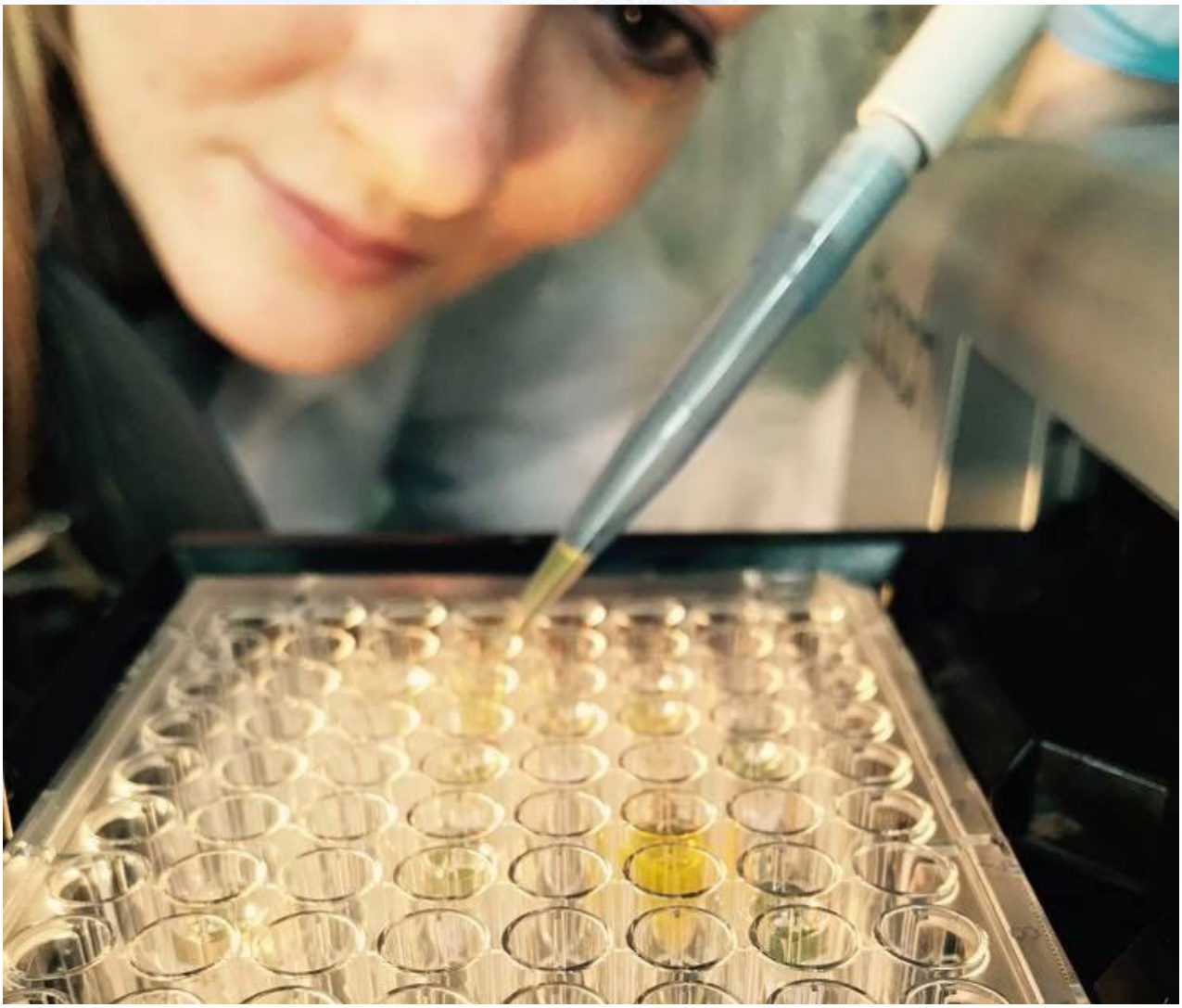


Fig. 2 Mgr. Katarína Janšáková, PhD., ARCA scientist, processes plasma samples from autistic children as part of research on sex hormones in the etiology of autism.

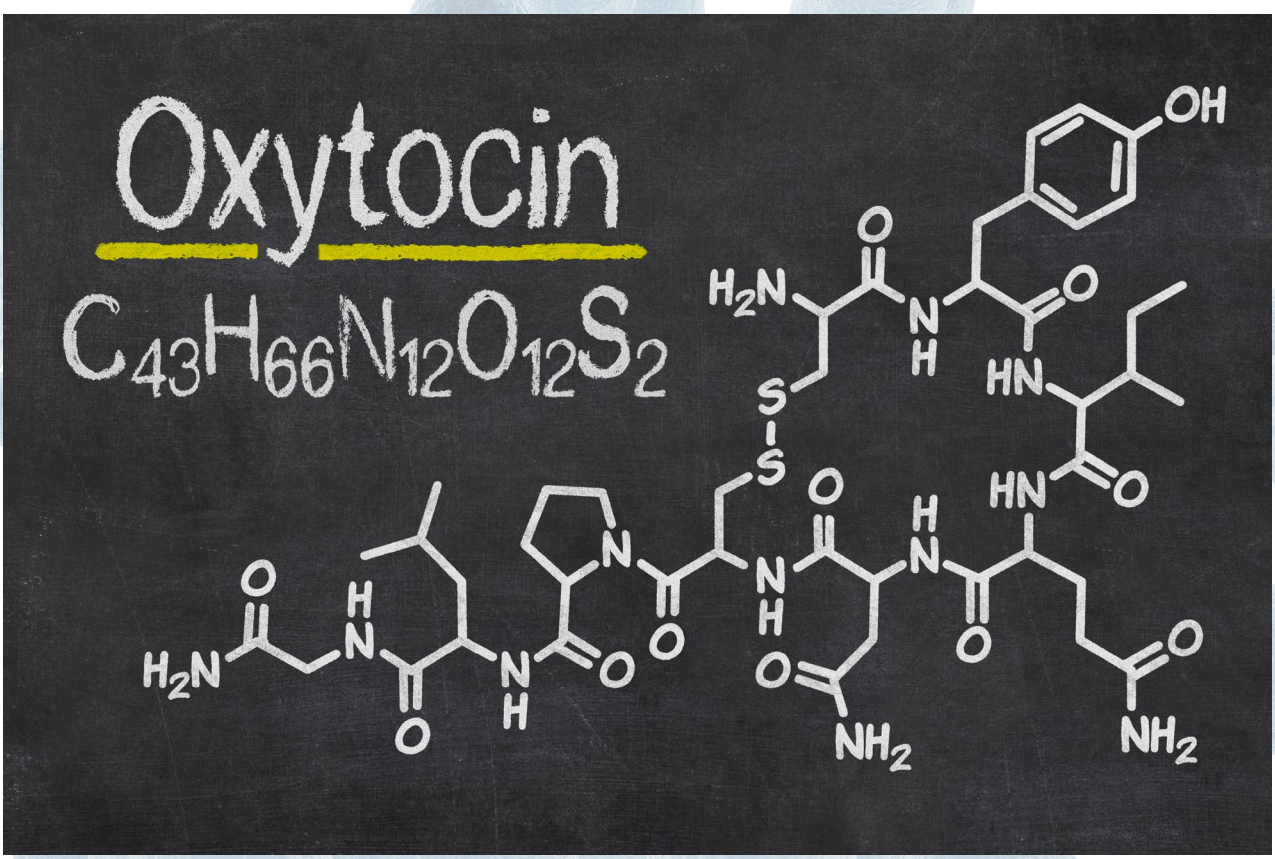
A problem of an autistic individual is closely related not only to different perception of appropriate sensory inputs, but in their bran processing as well. Simply, there is observed a filtra-tion failure of non-essential information and a problem of processing related to unpicked inputs coming from different sensory organs. As a result, the decision-making brain areas are being overloaded. An uncoordinated attention paid to detailed inputs generates chaos within hierarchical levels of cerebral cortex and this is denoted as a central coherence failure, while aiming to detail does not enable selecting and integrating information so that it could create a coherent and compact image. As a result of that, ASD individuals do not see a "forest because of a tree" and they do not have a capability of central coherence and they see their world in a set of fragments. Understanding autism etiology requires integration of three different levels – genetic, neurobiological, and neuropsychological.

Hormones as the autism potential biomarkers

In general, the boys are being diagnosed with autism more frequently (at about four times), than the girls are, while that ratio is being changed with respect to intellectual capacity of children as well. When considering the children with intellectual deficits a number of boys and girls seems to be quite equal. On the other hand, the ASD individuals having a higher or over average intelligence, indicate the ASD diagnosis more frequently (at about ten times) in boys than in girls. When looking for the explanation, there might be postulated more assumptions. There is considered a testosterone (male sex hormone) effect, which seems to be a significant brain developmental factor during intrauterine life. There might be postulated an assumption, that that hormone excess concentrations generate the brain hypermasculinization, which is represented by a high level of systematization (understanding, prediction, and creation of systems) and a low level of empathy (understanding of feelings of other people) and a low capability to react and to understand them as well. At present, the hyper-male brain theory has been extended to more general "fetal steroid theory", which postulates a fact that the autistic spectrum disorders risk factors are determined by testosterone increased concentrations, insufficient estrogen quantity or a changed ratio between estrogens and testosterone observed within prenatal period too. The boys with autism spectrum disorders indicated steroid trajectory disorders and that was confirmed within ARCA scientists as well. It is possible, there is another factor, we do not know a biological mechanism of it, which is protecting the female sex or enables better compensating that neurodevelopmental disorder. It means, that the girls need the higher genetic and environmental risk than the boys in order to have autism equally manifested. It is needed to make research related to autism indication symptoms related to both sexes in order to apply different diagnostic and intervention methods for boys and girls, respectively.

Oxytocin and vasopressin are neuropeptides being produced in the brain with sexually dimorphic effect and they affect the brain development and behavior. The oxytocin increased level observed in women have a protective effect against autism. On the other hand, the male brain is more sensitive to vasopressin regulation task. A high prevalence of autism in men might be caused by differences in endocrine regulations and in a different genetic equipment between both sexes. The increased levels of male sexual hormones might affect oxytocin effect, while vasopressin synthesis and its receptors depend on androgens as well.

A violation of that regulation might generate social behavior disturbances and increased anxiety level and creation of stereotype behavior, which seem to be the characteristic of autism. Oxytocin



and vasopressin fill their regulation task at the brain structure development and via binding to their receptors. The oxytocin and vasopressin are localized in those areas of the brain, which have a share related to social and reproductive behavior. However, there exits no proof, if the neurochemical actions play the primary role related to autistic spectrum disorders or they contribute only to the entire individual and specific image of individuals with autism based on the nervous systems.

Intestine microbes and autism – are there any common aspects?

The human organism contains a lot of bacteria, viruses, and other micro-organisms, which we live in a symbiose, however, the largest populations of microbes live in our intestines. They create a gastrointestinal ecosystem, which is an integral part of our immune system – defined as the intestine. The intestinal microbiota affects the distant organs including brain via a set of complex immunity mechanisms. The microorganism influence might be observed before the child is being born. The substances created by mother's microbiota penetrate to foetus body via placenta into blood and affect the brain development. An assumption might be postulated, which says that the gut microbial content of ASD people might be a cause of digestive and nutritional problems, which seem to be additional ones to behavioral aspects as well. Research of "gut-brain axis" brings a lot of information and a set of tools related to understanding and affecting our health.

The intestine seems to be the brain doorkeeper and a healthy gut microbiota has a great influence related to a correct function of blood-brain barrier, which maintains a sterile environment in the brain. The microorganisms communicate with brain via neurotransmitters coming from intestine and affecting the brain functions. The actual possibilities of microbiome sequencing

enable determining gut microbiota composition, what might indicate not only a diagnostic value but also a healing effect with the use of individually prepared probiotic or transplantation of the entire gut microbiota from healthy donors. This is an example of the precise medicine.

Fig. 3 The research on autism at ARCA is also provided by PhD students. Molecular biologists, geneticists, psychologists and anthropologists are interested in doctoral studies. One of them lectures at the Physiological days at the Jessenius Faculty of Medicine – Comenius University in Martin.

The behavioral interventions – a positive influence on core symptoms of autism

At present, no reliable biological marker is known, which could be investigated based on blood, urine, or other biological material in order to confirm autism. No drugs are known for the underlying symptoms of autism, nevertheless, evidence-based therapy via behavioral interventions is effective. An applied behavior analysis seems to be mostly applied early intervention, since it is evidence- based method modifying the behavior. However, there also is a wide scale of techniques and therapeutic methods concerned with autism based on behavior analysis, while availability of that therapy type in Slovakia is rather limited.

The above-mentioned evidence based symptomatic treatment applies behavior basic research knowledge, the aim of which is to minimize deficit consequences related to that type of disease and to help the child with autism spectrum disorder to improve functionality, self-service, learning capabilities and adaptive skills within social environment. It focuses in particular on expanding the repertoire of skills that are weakened during the primary diagnosis and eliminating or reducing the frequency of undesirable behaviors that may make it impossible to train and engage in

society, as well as to endanger their own health (e.g. self-harm). With respect to evidence-based medicine, the behavioral intervention is considered to be verified from scientific point of view as an efficient approach when looking for solutions of problematic behavior and development of communication social skills as well.

The intervention based on the applied behavior analysis should be provided individually, it means one child versus one therapist. It should be accommodated to the child development and a certified behavior analyst should prepare such intervention based on child functional status detailed analysis. If a functional analysis of problematic behavior is needed to be done, that analyst should check and control the analysis course as well, while the analysis outputs are being evaluated regularly and the intervention procedure is modified subsequently.

There are not sufficient number of behavioral intervention providers in Slovakia, when comparing it with a good clinical practice provided abroad, while an in-time intervention should be fixed based on behavioral analysis principles as an efficient tool for education of children with autism and it is important from patient management point of view as well.

Conclusion

The autism awareness in Slovakia is increasing from year to year. The reason is not only because of the Autism Awareness Day declared by WHO on April 2, 2007, but also thanks to many experts, lay persons and parents of children with autism who help to improve in time diagnostics and access to standard health care and therapies. However, the systematic care of ASD individuals in Slovakia is absent what is a global challenge as well, while it is necessary to increase the autism awareness, to support in time autism diagnostics via regular screening provided by pediatricians and to assure the subsequent diagnostics and appropriate evidence- based intervention.

The patients with autism should have access to standard health care and therapies related to accompanying diseases together with appropriate behavioral interventions, while their personality should also be fully respected. When considering the management of autistic individuals, there is an important aspect to apply a potential for their inclusion among healthy population and to provide an adequate education for them as well, while it is our common aim to assure the better life quality for them and their families.

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The supplementary studying article sequence is being ordered with respect to the contribution chapters.

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MÁME DIEŤA S AUTIZMOM

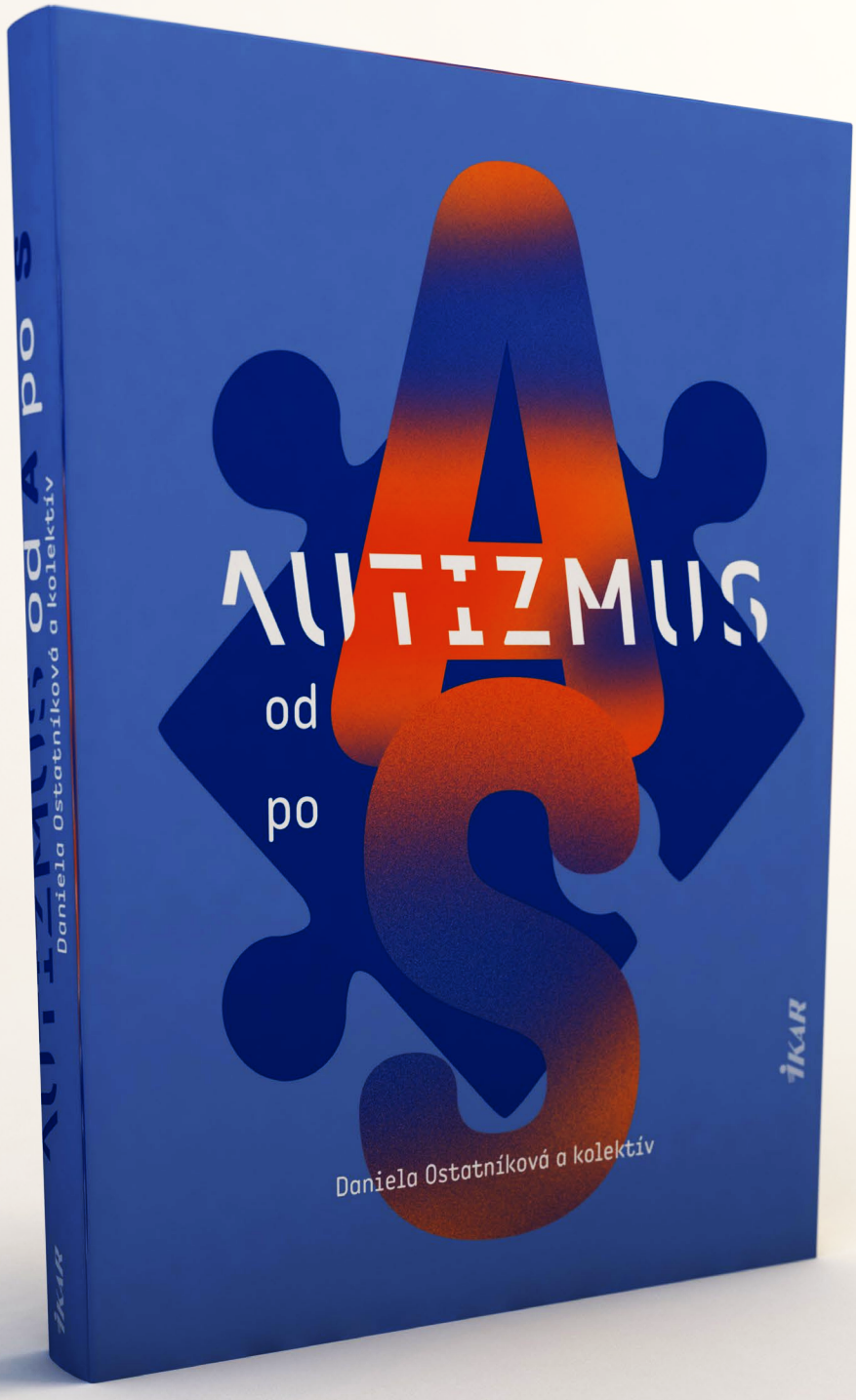
DANIELA OSTATNÍKOVÁ
a kolektív autoriek

kompas
pre rodičov

Vydané z prostriedkov
Nadácie Krištáľové krídlo®

Celosvetové údaje o náraste autizmu za posledné desaťročia sú alarmujúce. Výskyt jedného dieťaťa s autizmom do veku 8 rokov na 100 detí daného veku prisudzuje tomuto ochoreniu epidemický charakter. Ani na Slovensku nezostávame k týmto štatistikám nevšímaví... Aj keď sa stále nedarí presne identifikovať pôvod tohto ochorenia, jedno vieme isto, že správnou a včasnou diagnostikou a následnou odbornou pomocou možno dosiahnuť funkčný stav dieťaťa s autizmom, dokonca v tých najúspešnejších prípadoch porovnateľný so zdravými deťmi. Podmienkou akejkoľvek intervencie je okrem správnej diagnózy aj identifikácia sprievodných ochorení. Efektívna medicínska liečba komorbidít je nevyhnutnou podmienkou pre behaviorálnu liečbu. Zlepšenie fyzického zdravotného stavu detí s autizmom totiž výrazne zvyšuje ich vnímavosť na behaviorálne intervencie a následne aj šance na ich úspešnosť. Liečba symptómov autizmu založená na aplikovanej behaviorálnej analýze (ABA) má v súčasnosti najvyššiu šancu na maximalizáciu potenciálu dieťaťa s autizmom.

Autorky tejto knižky chcú formou odpovedí na najčastejšie kladené otázky rodičov a odborníkov poskytnúť najnovšie overené a dostupné informácie, a tak im dať do rúk „kompas“ podľa ktorého sa správne a rýchlo budú môcť zorientovať a problém, ktorý má všeobecný názov autizmus, aj efektívne riešiť. Celou knižkou sa tiahne základná myšlienka pomôcť slabším pretavená do kresbičiek inšpirovaných de Saint-Exupéryho Malým princom...



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April 2, 2022

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