

INTESTINAL MICROBIOME SHIFTS IN CHILDREN WITH DIFFERENT SEVERITY OF AUTISM

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ABSTRACT

The aim of the study was to describe detailed composition of the intestinal microbiome of children with autism spectrum disorders (ASD). The study was observational, cohort, comparative. All the patients were divided into 2 groups. The first (main) group (n=46) consisted of children aged 4.92 ± 1.57 years with an established diagnosis of ASD. The second (n=20, comparison group) included conditionally healthy children (1 and 2 health groups) aged 5.10 ± 1.16 years, not suffering from ASD. The study showed that in children with ASD, the presence of significant differences in the qualitative and quantitative composition of the intestinal microbiota was established according to the study of feces for dysbiosis. The taxonomic composition of the microbiome of patients with ASD as in healthy included 4 types of bacteria: Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria, but ASD children had low level of the type of Firmicutes. In opposite, the type of Actinobacteria was elevated in this disease.

Keywords: autism, children, gut microbiota, dysbiosis

INTRODUCTION

Currently, there is a tendency to increase the prevalence of autism in the world [1-3]. However, international and local data do not reflect the true scale of the problem of the prevalence of autism spectrum disorders (ASD) due to the difficulty of diagnosing and registering such conditions, heterogeneity of health organization systems around the world, etc. The results of a few epidemiological studies of ASD in the Russian Federation, obtained during screening pilot projects, showed that the condition of pre-disease (risk of ASD) in children aged 16-24 months is 103.5 cases per 1000 [4].

ASD is characterized by a large number of comorbid conditions affecting various other organs and systems. Thus, pathological conditions of the gastrointestinal tract (gastrointestinal tract) are described as the most common among concomitant diseases in patients with ASD [5]. In our previous studies, it was shown that children with ASD are significantly more likely than healthy children to show signs of dysbiosis, but a full-fledged analysis of the intestinal microbiota has not been performed [6].

The **aim of the study** was to describe detailed composition of the intestinal microbiome of children with autism spectrum disorders (ASD).

MATERIAL AND METHODS

The study was pilot, observational, cohort, comparative; conducted in 2 groups: the first (main) group (n=46 patients) consisted of children aged 4.92 ± 1.57 years with an established diagnosis of ASD; the second (n=20, comparison group) included conditionally healthy children (1 and 2 health groups) at the age of 5.10 ± 1.16 years, not suffering from ASD.

The diagnosis of ASD was verified according to the examination of a psychiatrist using ADOS and ADIR.

The examination of children of both groups included the collection of complaints, an objective examination by a pediatrician, a bacteriological study of the qualitative and quantitative composition of the intestinal microflora, interviewing the mother/guardian of the child using a questionnaire "Studying the medical and social causes of the formation of health abnormalities and diseases in children", the answers to which reflected the presence/absence of biomedical factors in the child risk of maternal pregnancy and childbirth; risk factors of early childhood and risk factors associated with the child's living conditions.

Statistical data processing was carried out using the Statistika 6.0. for Windows application software package. Parametric and nonparametric statistics were used.

RESULTS

The presence of functional disorders and/or diseases of the gastrointestinal tract in children with ASD was indicated by the presence of dyspepsia syndrome, which was manifested by complaints of decreased appetite (25.0%, $p=0.014$); a tendency to stool retention/constipation (39.0%, $p=0.005$), including in a third (33.3%) - with a delay in defecation up to 3-7 days; the presence of a tight "fragmented" and/or dry and/or "lumpy" stool (33.3%, $p = 0.015$); the presence of undigested pieces of food in the feces of the child (25.0%, $p = 0.056$); periodic dilution of stool (5.0%, $p > 0.050$) and episodes of the presence of pathological impurities in it in the form of mucus / blood (2.0%, $p > 0.050$). Children with ASD were characterized by the most frequent detection of intestinal dysbiosis in general ($p=0.019$) and the detection of significant dysbiotic disorders in the form of intestinal dysbiosis of 3-4 degrees ($p=0.049$).

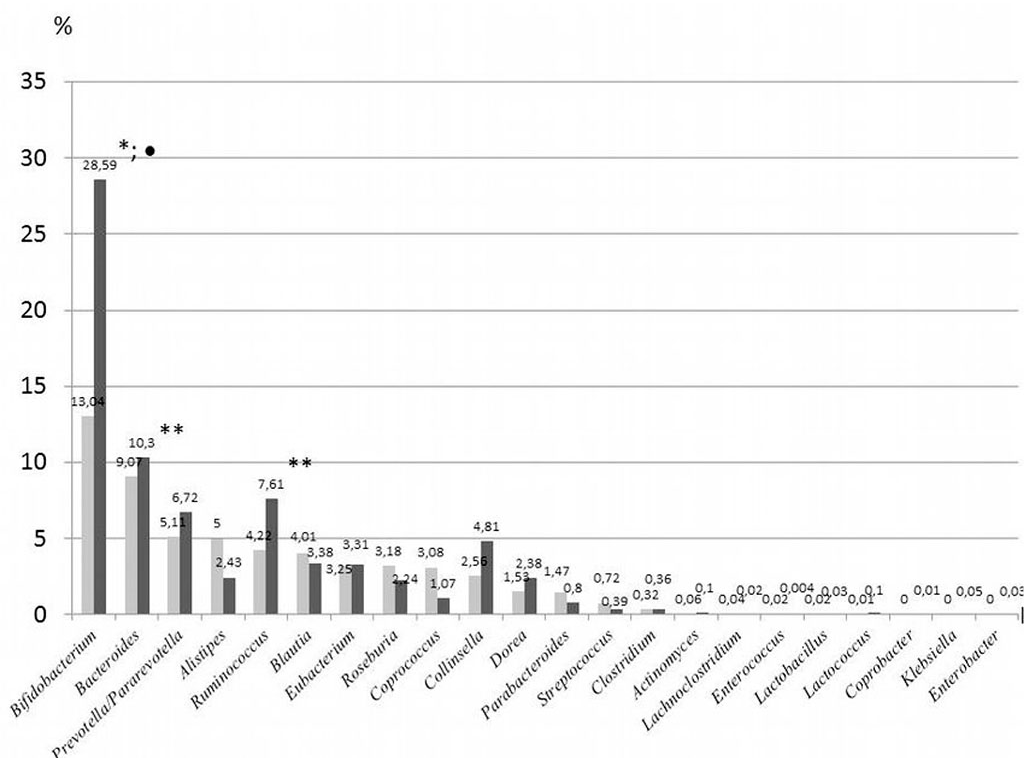


Figure 1. Intestinal microbiome (common type) components in healthy children (light columns) and children with ASD (dark columns) [*- statistical significance of differences in comparison with the types of Bacteroidetes and Proteobacteria ($0.001 \leq p \leq 0.030$); **- statistical significance of differences in the representation of the corresponding type with the group of healthy ($p=0.023$)]

The qualitative and quantitative composition of the intestinal microbiota in patients with ASD differed

significantly from that in children in the comparison group.

The use of intelligence regression analysis made it possible to identify certain types of intestinal microbiota bacteria and their "communities" associated with the severity of autistic disorders in scores according to ADOS and ADIR data.

The taxonomic composition of the microbiome of patients with ASD as in healthy included 4 types of bacteria: Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria, but ASD children had low level of the type of Firmicutes. In opposite, the type of Actinobacteria was elevated in this disease (Fig. 1).

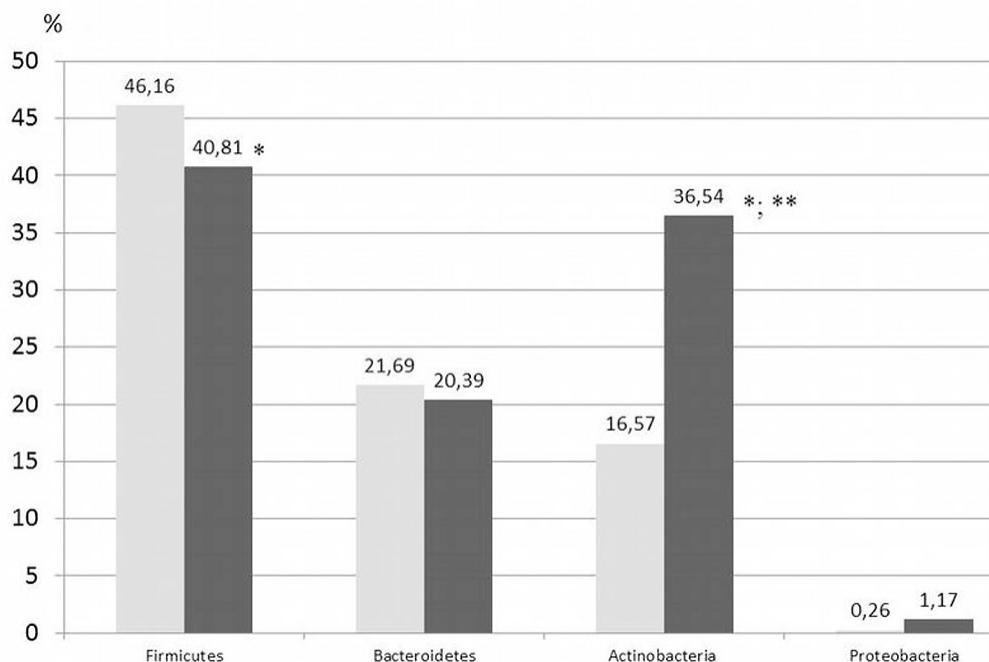


Figure 2. Intestinal microbiome (genus classification) components in healthy children (light columns) and children with ASD (dark columns) [- statistical significance of differences within the group with ASD compared to all the genera presented ($0.001 \leq p \leq 0.004$); ** - statistical significance of differences within the group with ASD with genera Alistipes, Blautia, Eubacterium, Roseburia, Coprococcus, Collinsella, Dorea, Parabacteroides, Streptococcus, Clostridium, Actinomyces, Lachnoclostridium, Enterococcus, Lactobacillus, Lactococcus, Coprobacter, Klebsiella and Enterobacter ($p < 0.05$); • - statistical significance of differences between groups ($p < 0.05$)]*

The generic representation of the taxonomic composition of the microbiome (Fig. 2) in ASD differed from that in healthy children: the genus Bifidobacterium dominated ($28.59 \pm 21.86\%$, $0.001 \leq p \leq 0.004$ within the group with ASD, $p = 0.047$ compared with the healthy group); equally represented ($p > 0.05$) genera Bacteroides ($10.30 \pm 10.79\%$) and Ruminococcus ($7.61 \pm 7.07\%$) prevailed over all the genera presented ($0.001 \leq p \leq 0.020$ and $0.001 \leq p \leq 0.037$, respectively), except for bacteria of the genus Bifidobacterium and Prevotella/Paraprevotella ($p > 0.05$).

CONCLUSION

In children with ASD, the presence of significant differences in the qualitative and quantitative composition of the intestinal microbiota was established according to the study of feces for dysbiosis. The taxonomic composition of the microbiome of patients with ASD as in healthy included 4 types of bacteria: Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria, but ASD children had low level of the type of Firmicutes. In opposite, the type of Actinobacteria was elevated in this disease.

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