Gut-brain axis dysfunction in Autism Spectrum Disorder Affected by Microbiota & Metabolic Network

Mohammadamin Mahmanzar*[1], Javad Zahiri[1], Seyed Shahriar Arab[1]

[1]- *Department of Biophysics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran*

E-mail: mahmanzar74@gmail.com

Objective and background:

Autism Spectrum Disorders (ASD) is a box of colored pencils containing various types of Spectrum. The global prevalence of ASD showed that One in every ١٠٠ people had been affected by ASD, and rates have shown an increasing trend over time. This group of disorders Has become a major concern in the community and education, leading families and government to pay high education and training costs. (Lasheras et al., ٢٠٢٠)

Interestingly the prevalence of gastrointestinal disease is significantly higher in autistic children versus normal children. Several studies recently demonstrated that the composition of the intestinal microbiota in ASD individuals, often reported under the controversial term "dysbiosis, " provides a reasonable response for the more frequent occurrence of functional GI disorders.(Lasheras et al., ٢٠٢٠; Nitschke, Deonandan, & Konkle, ٢٠٢٠)

Following studies have been reports of a direct association between metabolites produced by microbiota and neurological diseases. This means that microbiota could affect the brain
functions and development through the gut-brain But it is noteworthy that characterization
A distinctive ASD microbial pattern and its possible role in ASD remains unclear.

The gut microbiome consists of more than ١٠٠ trillion microorganisms, containing bacteria and viruses on a large scale. On a small scale, fungi and protozoa exist. Due to the development of high throughput sequencing of ١٦S rRNA gene amplicon and shotgun metagenomic sequencing, understanding the role of microbiomes in causing disease became clearer tremendously over the past decade(Verhaar, Prodan, Nieuwdorp, & Muller, ٢٠٢٠). Gut microbiota composition is largely influenced by dietary factors, Delivery mode, Early feeding pattern, Maternal Gestational Diabetes, obesity during pregnancy, and Antibiotics. This difference in the microbiota population leads to the production of more or fewer metabolites essential for the health of the nervous system. Altogether, the present study highlighted the alternation pattern of bacteria in ASD children and found the key metabolite which plays a critical role in autism pathogenesis pathways.

Keywords:

Early detection, Microbiome, Autism Spectrum Disorder, Metabolite

Methodology:

Based on keywords, Microbiota, Autism Spectrum Disorders, and Diagnosis searched articles in the valid database, PubMed and Scopus. For screening, In the first step, the titles and the second phase, abstracts were reviewed. All articles were evaluated based on included and excluded criteria. The more relative studies were imported and ignored with excluding criteria such as animal models, behavioral studies, and other diseases. After that, text-minded the literature and the significant bacteria with alternation status were visualized in Figure ١. used microbiomology.org database To extract the produced or consumed bacteria metabolites common between them and play a Hub role. A Heatmap was drawn to Visualized the correlations between metabolite and bacteria by R ٣،٨ programming language, package pheatmap, and ggplot. Common metabolites were extracted and used in the Human metabolome database (https://hmdb.ca/) to obtain a unique metabolite id. Ultimately, to find the functional correlation between these metabolites, perform Pathway analysis using an integrated molecular pathway-level analysis database(http://impala.molgen.mpg.de/).

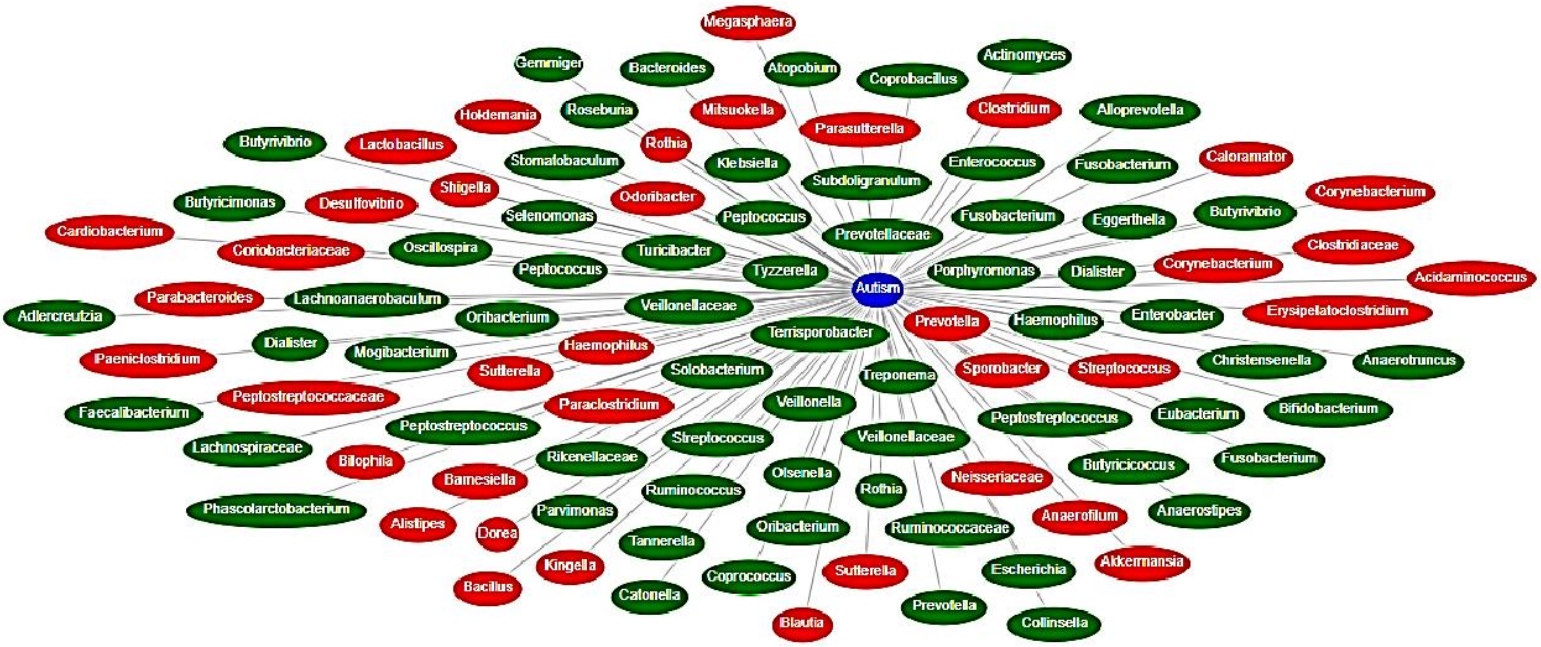

Fig١. Bacteria alternation in ASD. Selected bacteria with significant demographic pattern changes in ASD. Red: Decrease, Green: Increase

Results:

Based on the study strategy, we found ١٤٦ articles by mentioned keywords, including ٥٨ articles Following our criteria. Sixty-nine bacteria with significant alternation in fecal were selected. An average of ٩٠٠ to

۲۰۰۰ metabolites were identified for each bacterium. The circular heat map diagram in Figure ۲ shows the ۱٦٤ common metabolites between the ٦۹ selected bacteria. In the last part, ٦٤ pathways were identified, from which ۱۹ pathways have a p-value <۰,۰٥ Fig۳.

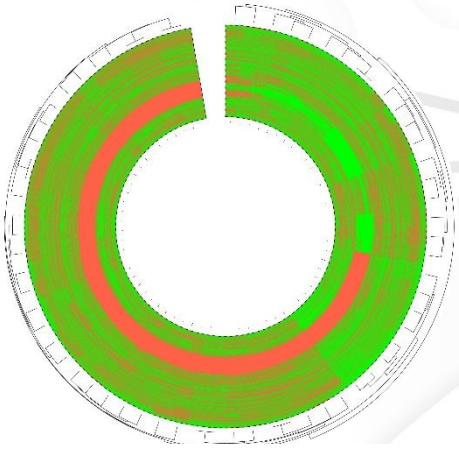

Fig۲. Metabolite Hetamap. This heatmap shows prevalence of metabolite in ٦۹ bacteria.

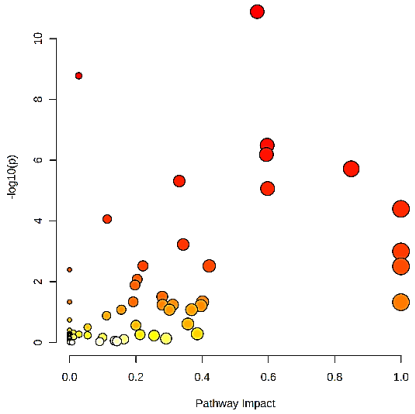

Fig۳. Detected pathways. Detected pathways. The level of selected metabolite contribution distinctly relates to the size of dots

Conclusions:

Diagnosis of autism is difficult due to the lack of clinical symptoms from birth to ۷ years. In order to diagnose this disease, the psychiatrist has to perform various tests such as behavioral to comment on whether or not the child has autism. On the other hand, the wide range of this disease makes it doubly difficult for a doctor to diagnose the disease. This has led to a lack of specific and standard treatment methods. The present study examines how the intestinal bacteria of children with autism diversify in the first step to discover the biological pathways involved in the pathogenesis of this disease. The discovery of key metabolites and providing a diagnostic framework for the physician could pave the way for proposing new therapies for the treatment of this disease

References:

References should be listed in alphabetical order and presented in a format presented in the conference website (style download: in the call for paper page below this English template) according to the following: (Heirendt et al. ۲۰۱۹)

Heirendt, Laurent, Sylvain Arreckx, Thomas Pfau, Sebastian N Mendoza, Anne Richelle, Almut Heinken, Hulda S Haraldsdottir, Jacek Wachowiak, Sarah M Keating and Vanja Vlasov. "Creation and Analysis of Biochemical Constraint-Based Models Using the Cobra Toolbox V. ۳,۰." *Nature protocols* ۱٤, no. ۳ (۲۰۱۹): ٦۳۹.