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UNDERSTANDING GUT HEALTH IN CHILDREN WITH AUTISM: NEW PERSPECTIVES AND THERAPEUTIC STRATEGIES

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ABSTRACT

Autism Spectrum Disorder (ASD) encompasses a range of neurodevelopmental traits that influence perception, communication, and social interaction, often accompanied by restricted behaviors and sensory sensitivities. This overview examines the relationship between ASD and gastrointestinal (GI) issues, which frequently co-occur and significantly impact quality of life for affected individuals. Gastrointestinal problems including constipation, diarrhea, and food sensitivities are commonly observed in children with ASD. These issues likely result from multiple interacting factors such as microbiota dysbiosis, immune dysregulation, intestinal hyperpermeability, and dietary patterns. Research has identified disrupted gut microbiome profiles in children with ASD, with increased presence of pathogenic bacteria and associated immune reactivity, including anti-gliadin antibodies. Diagnosing GI disorders in individuals with ASD remains challenging due to communication barriers and atypical sensory processing, with no standardized diagnostic methods currently available. Treatment approaches focus on microbiota restoration through dietary modifications, probiotics, and emerging therapies like Microbiota Transplant Therapy (MTT). Recent studies of MTT have demonstrated sustained improvements in both GI and behavioral symptoms, suggesting promising directions for future interventions that address both the gastrointestinal and behavioral aspects of ASD. Further research is needed to develop standardized diagnostic protocols and evidence-based treatments for this population.

KEYWORDS

Autism Spectrum Disorder, Gastrointestinal Disorders, Microbiome, Gut Dysbiosis, Immune Dysregulation

CITATION

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Introduction.

Autism spectrum disorder (ASD) presents as a complex constellation of neurodevelopmental traits that fundamentally alter an individual's perception, communication patterns, and capacity for social engagement [1, 2, 19]. The condition is characterized by restricted and repetitive behaviors, intense interests, and hypersensitivity to sensory stimuli [3]. Children with ASD frequently experience various medical issues affecting multiple organ systems, including the neurological, immune, and gastrointestinal systems [5, 6]. Among these, gastrointestinal (GI) problems—such as constipation, diarrhea, food sensitivities, and digestive difficulties—are particularly common and can significantly impact quality of life [7, 8]. Constipation stands out as the most prevalent GI issue reported in individuals with ASD [13, 14, 18]. Research indicates that children on the autism spectrum experience gastrointestinal issues at least three times more frequently than neurotypical children. [24, 26]

The etiology of these GI issues remains incompletely understood; however, growing evidence suggests they arise from a complex interplay of factors, including genetic predispositions, immune dysregulation, alterations in the gut microbiome, and even psychiatric comorbidities such as anxiety and stress [5, 7, 12, 19].

The gut-brain axis represents a bidirectional communication pathway connecting the brain and GI system [4, 11, 30]. The gut microbiota plays a crucial role in this axis, influencing brain activity through various signaling mechanisms [16, 17, 22]. Conversely, the brain affects gut microbiota composition via neurotransmitters like serotonin and dopamine, as well as stress hormones such as cortisol [4]. The gut communicates with the brain through multiple pathways, including vagus nerve stimulation, immune system signaling, and neurotransmitters such as leptin and serotonin, supported by factors like mucosal barrier integrity and short-chain fatty acids including butyrate [4, 11, 17, 30].

This intricate relationship underscores the need for an integrated approach to understanding and managing these challenges in children with ASD [8, 16].

Materials and Methods

A focused literature review was conducted to explore gastrointestinal (GI) issues in children with Autism Spectrum Disorder (ASD). The search was performed using databases such as PubMed, Google Scholar, and Elsevier, employing the following keywords:"gastrointestinal symptoms in autism, ""GI disorders in ASD, ""gut microbiota and autism, " and"gastrointestinal treatment in children with ASD." Only English-language publications were included. Additional relevant studies were identified through manual screening of reference lists from selected articles. All retrieved papers were evaluated for relevance based on their titles, abstracts, and full-text content. We used AI tools to grammatically correct text.

Discussion

Among the challenges faced by children with ASD, gastrointestinal disturbances emerge as particularly prevalent, with studies reporting incidence rates varying from 8% to 91% of caes [7, 12]. The causes of these problems are not clearly defined. It is believed that gastrointestinal issues are multifactorial in nature [5, 8]. One of the suggested causes is microbiota dysbiosis in children with ASD [9, 10]. Studies have shown a higher prevalence of pathogenic bacteria, such as Clostridia C. boltae, C. hystoliticum, C. perfringens in children with ASD compared to neurotypical children [6, 11, 27]. Gut microbiota can influence the central nervous system (CNS) through various mechanisms, including indirect effects on the innate immune system [4, 16, 20]. These effects occur via circulating pro-inflammatory and anti-inflammatory cytokines or through metabolites, such as short-chain fatty acids (SCFAs), which regulate both the immune and sympathetic nervous systems [11, 17].

Another cause reported in studies is intestinal hyperpermeability, and heightened immune reactivity [5, 8]. This condition is believed to play a significant role in the gastrointestinal issues observed in children with ASD [6, 8]. These children are often characterized by notable food selectivity, frequently favoring foods rich in gluten and casein, which can exacerbate gut-related problems [12, 13]. Research has consistently shown that children with ASD often experience malabsorption and increased intestinal permeability, both of which can lead to systemic inflammation and disrupt normal digestive function [8, 11]. Additionally, studies suggest a potential link between these symptoms and the presence of anti-gliadin antibodies, which are produced as a result of immune system reactivity to gluten [5, 12]. This immune response may further aggravate gastrointestinal symptoms and contribute to a cycle of inflammation and gut dysfunction, highlighting the complex interplay between diet, immune activity, and gut health in ASD [11, 12].

Although children on the autism spectrum exhibit significantly elevated stress levels, accompanied by increased cortisol and pro-inflammatory cytokines [5], studies have not demonstrated a clear link between these factors and gastrointestinal disorders [14]. Despite the biological plausibility of such a connection, the existing research has yet to establish a definitive association, suggesting that the relationship between stress-related biomarkers and gastrointestinal issues in ASD may be more complex than initially assumed [5, 14].

Diagnosis

The Rome Criteria are considered the gold standard for diagnosing gastrointestinal disorders in pediatric population [12, 14]. It consists of 7 items addressing symptoms such as constipation, diarrhea, stool consistency, stool odor, flatulence, gas, and abdominal pain [14]. The tool assesses both abdominal symptoms (e.g., abdominal pain, gas, constipation) and gastrointestinal symptoms related to vomiting and defecation (e.g., vomiting, inappropriate defecation, diarrhea, rumination) [12, 14]. Each item is rated on a four-point Likert scale, ranging from 0. Therefore their use requires effective communication and cooperation with the child [7, 13]. Due to communication challenges, applying them to children on the autism spectrum is significantly more difficult [7, 12, 25]. Limited verbal abilities often observed in children with ASD and, even when verbal skills are intact, atypical sensory perception, can make it challenging for them to identify the pain or cause of discomfort [7, 13].

Recent research has emphasized the importance of developing more comprehensive diagnostic approaches specifically tailored to the ASD population [13, 14, 21]. Current diagnostic protocols often incorporate multiple assessment tools, including behavioral observation scales, parent-reported questionnaires, and physiological measurements [7, 12, 25]. Medical professionals increasingly recognize the need for a multimodal approach to diagnosis, combining traditional gastrointestinal assessment methods with ASD-specific behavioral markers [12, 13, 26].

Diagnostic process can be challening due to the idiosyncratic manifestation of gastrointestinal symptoms in the ASD population, where traditional symptomatic indicators may be obscured by communication barriers. Research has shown that these children may express gastrointestinal discomfort through various behavioral

manifestations, including increased stereotypical behaviors, aggression, self-injurious behaviors or sleep problems [5, 13, 26]. This atypical presentation necessitates careful observation and interpretation of behavioral changes as potential indicators of underlying GI issues [13, 14]. Behavioral changes are particularly important to observe during the diagnostic process, as parents of children with ASD may have difficulty accurately identifying or reporting gastrointestinal symptoms. [25]

Specialized questionnaires tailored to children with ASD have been developed [7, 12]. ATEC subscale, ATN Gastrointestinal Symptom Inventory, CHARGE GIH questionnaire, Parental Concerns Questionnaire, and ATN Diagnoses and Problems form were adapted for children with ASD and specifically validated for this population [7, 12]. Advanced diagnostic techniques, such as wireless motility capsules and specialized imaging studies, are being increasingly utilized to provide more objective measures of gastrointestinal function in cases where traditional diagnostic methods prove insufficient [8, 12]. Nonetheless, the authors of this article suggest that there is no standardized method for diagnosing gastrointestinal disorders in children on the autism spectrum [7, 13, 23]. As a result, many affected children remain undiagnosed and do not receive appropriate treatment. Future research should focus on addressing this gap. [26]

Treatment

Diagnosing and treating gastrointestinal (GI) disorders in children with ASD is of critical importance, as these issues can significantly impact both physical health and behavioral outcomes [8, 13, 25]. Research has established a link between GI problems, particularly constipation, and an increase in rigid and compulsive behaviors commonly observed in children with ASD [13, 14]. Addressing these GI issues is therefore not only essential for improving physical comfort but also for potentially alleviating some behavioral symptoms [2, 8].

Current therapeutic approaches prioritize restoring and maintaining a healthy balance in the gut microbiome [9, 10]. Numerous studies have explored the potential benefits of interventions such as chronic probiotic administration and Microbiota Transplant Therapy (MTT) in managing GI disorders [10, 15, 16]. While these methods show promise, they are often complemented by dietary modifications, which play a crucial role in gut health [8, 12]. A well-balanced diet, emphasizing the appropriate proportions of carbohydrates, proteins, and fats, has been proven to influence the structure and diversity of the gut microbiome [6, 8]. Together, these strategies aim to create a multifaceted approach to managing GI disorders in children with ASD, addressing both immediate symptoms and their underlying causes [8, 16].

The most promising method, supported by scientific research, appears to be Microbiota Transplant Therapy (MTT) [9, 10, 15]. The therapy aims to restore a balanced microbiome composition by transferring gut microbiota from the feces of healthy donors into patients [10, 15]. MTT is preceded by a two-week course of vancomycin therapy [9, 10].

A study to observe symptoms and the diversity of their gut bacteria after a two-year period following MTT was conducted [9, 10]. Two years after treatment, participants reported a sustained 58% reduction in GI symptoms based on the Gastrointestinal Symptom Rating Scale (GSRS) [10]. Behavioral improvements were also significant. On the Childhood Autism Rating Scale (CARS), professional evaluators recorded a 47% reduction in ASD severity compared to baseline, with 83% of participants initially classified as severe ASD dropping to only 17% in this category at follow-up [9, 10]. Alterations in gut microbiota also were sustained after two years [10].

Recent advances in pharmacological interventions have focused on targeting specific aspects of gut dysfunction [8, 11]. Selective serotonin reuptake inhibitors (SSRIs), traditionally used for managing anxiety and depression, have shown promise in addressing both gastrointestinal and behavioral symptoms in ASD [5, 8]. This dual effect is thought to be mediated through the modulation of enterochromaffin cells, which are major producers of peripheral serotonin and play a crucial role in gut motility and secretion [8, 11]. Additionally, novel pharmaceutical compounds targeting specific gut-brain axis pathways, such as 5-HT4 receptor agonists and mast cell stabilizers, are currently under investigation in clinical trials [8, 16].

Furthermore, emerging research has highlighted the potential therapeutic value of specialized dietary interventions in managing GI symptoms in children with ASD [8, 12, 27]. The gluten-free casein-free (GFCF) diet has garnered particular attention in recent scientific literature [8, 12]. This dietary approach is predicated on the opioid excess theory, which posits that individuals with ASD may have abnormal metabolism of gluten and casein proteins, leading to the formation of opioid-like peptides that can affect both gastrointestinal function and neurological activity [5, 12]. Studies utilizing high-performance liquid chromatography (HPLC) have detected elevated levels of these peptides in the urine of children with ASD, suggesting a potential

metabolic basis for dietary intervention [12, 27]. Dietary protein components may directly impact the gut-brain axis through the formation of bioactive peptides that influence neurological function. [27]

Studies have not demonstrated a consistent effect of regular probiotic use as a standalone treatment for gastrointestinal disorders. [16, 29]. However, specific strains, such as *Lactobacillus rhamnosus*, have shown potential effects beyond the gut [4, 16]. Research indicates that *L. rhamnosus* can influence the GABA-ergic system, which plays a role in regulating emotional state and behavior [4, 28]. This strain has been associated with positive effects on behavioral symptoms in individuals with ASD, including a reduction in anxiety and depression symptoms [4, 28]. Although the use of probiotics in ASD is not scientifically confirmed as an established treatment, studies have shown that probiotics may affect intestinal permeability and immune system function, potentially contributing to the management of core factors underlying GI symptoms in ASD. [4, 20, 28]

As previously mentioned, children with ASD have a disrupted gut microbiome, characterized by the presence of numerous pathogenic bacteria [6, 10, 11]. There was a study that proved specific alterations in the gut microbiota of individuals with ASD, including reduced levels of Bacteroidetes and increased levels of Firmicutes compared to neurotypical controls[30]. A study, in which children were administered vancomycin for 8 weeks, was conducted [9, 10]. Initially, the neurological functions of the children showed improvement; however, the effects were not sustained over the long term [10]. Not even the use of probiotics following the therapy resulted in lasting improvements in the children's health [10, 16]. The studies demonstratee that antibiotic therapy alone, even when administered over a prolonged period, is insufficient to achieve lasting resolution of gastrointestinal disorders in children with ASD [9, 10, 16]. One study has that different immune responses and microbiota profiles exist in children with ASD and co-morbid GI symptoms, suggesting that personalized therapeutic approaches may be more effective than standardized interventions. [29]

Conclusions

In children with Autism Spectrum Disorder (ASD), gastrointestinal (GI) pathologies represent a significant and often underrecognized comorbidity that not only impacts physical health but may also influence the severity and expression of core ASD behaviors. These disturbances—ranging from constipation and diarrhea to food sensitivities and malabsorption—are increasingly understood as the result of a complex, bidirectional interplay among altered gut microbiota composition, immune dysregulation, increased intestinal permeability, and specific dietary patterns commonly observed in this population.

Despite growing awareness, diagnosing GI issues in individuals with ASD remains fraught with difficulty, largely due to atypical symptom presentation and communication barriers. The lack of standardized and ASD-adapted diagnostic tools contributes to underdiagnosis or misdiagnosis, which can delay appropriate treatment and exacerbate behavioral and emotional distress in affected children. Thus, there is an urgent need for diagnostic protocols that are not only physiologically sensitive but also behaviorally attuned to the ASD phenotype.

Therapeutically, interventions targeting the gut microbiome have emerged as especially promising. Microbiota Transfer Therapy (MTT), in particular, demonstrates potential for durable improvement not only in GI symptoms but also in behavioral domains central to ASD. The sustained benefits observed up to two years post-treatment underscore the long-term therapeutic value of addressing gut dysbiosis. Other approaches, such as the use of specific probiotics, serotonin-modulating medications, and targeted dietary interventions like the gluten-free, casein-free (GFCF) diet, offer complementary strategies that merit further clinical exploration.

Future research should prioritize the development of comprehensive, multimodal diagnostic frameworks tailored to children with ASD, incorporating behavioral cues, physiological assessments, and novel biomarkers. Longitudinal studies are needed to elucidate the causal relationships among gut health, immune status, and neurodevelopmental functioning. Furthermore, randomized controlled trials investigating the safety, efficacy, and mechanisms of microbiome-focused therapies will be crucial to advancing evidence-based practice in this area.

Ultimately, a more nuanced understanding of the gut-brain-immune axis in ASD has the potential to transform clinical management, improve patient outcomes, and enhance quality of life for individuals and families affected by this complex condition.

Disclosure

Authors' contribution:
Conceptualization: JK, GŁ
Methodology: PK,
Software: KD, MB
Check: JM, JZ
Formal analysis: PK, KD
Investigation: Resources: MM, MB
Data curation: JK, KM
Writing- rough preparation JK
Writing - review and editing: GŁ, JZ, AN
Visualization: GŁ, MM
Supervision: AN, JM
Project administration: MM MB

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