The Relationship Between Inflammatory Bowel Disease and Autism Spectrum Disorder in Children

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Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disorder. In addition to core symptoms such as social impairments and repetitive stereotyped behaviors, nearly half of ASD patients exhibit gastrointestinal symptoms, manifesting as inflammatory bowel disease (IBD). IBD is a chronic disease associated with immune dysregulation, alterations in the gut microbiome, micronutrient malabsorption, and anemia; these features may represent perinatal factors associated with ASD. Children with ASD are likely to be diagnosed with comorbid conditions including IBD. Therapeutic approaches targeting IBD to alleviate or intervene in childhood ASD have demonstrated preliminary efficacy, and further clinical trials are warranted to confirm the efficacy and safety of IBD treatment. Investigations into the relationships between IBD and ASD, as well as between parental IBD and childhood ASD, can provide further evidence for etiological research, early screening, and clinical treatment of childhood ASD.

Full Text

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Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental condition. In addition to core symptoms including social impairments and restricted repetitive

behaviors, about half of individuals with ASD also experience gastrointestinal symptoms and inflammatory bowel disease (IBD). IBD is a chronic disease associated with immune dysregulation, gut microbiome alterations, micronutrient malabsorption, and anemia, which may be perinatal factors related to ASD. Children with ASD are likely to be diagnosed with comorbidities including IBD. Treating IBD to alleviate or intervene in childhood ASD has shown initial success, and future clinical trials should be conducted to verify the effectiveness and safety of IBD treatment. Investigating the relationships between IBD and ASD, as well as between parental IBD and childhood ASD, can provide further evidence for etiological research, early screening, and clinical treatment of childhood ASD.

Keywords: Autism spectrum disorder, inflammatory bowel disease, Crohn's disease, ulcerative colitis

Autism spectrum disorder (ASD) is a heterogeneous and heritable neurodevelopmental condition characterized by core symptoms including varying degrees of impaired social behavior, communication and language deficits, repetitive behaviors, and restricted interests and activities (Desalegn et al., 2023), accompanied by abnormalities in sensory perception, emotion, and affect (Duan et al., 2015). According to the 2010 Global Burden of Disease Study, an estimated 52 million people worldwide have ASD, equivalent to 7.6 per 1,000 individuals (Baxter et al., 2015). Domestic reports on ASD prevalence indicate that China's ASD prevalence is comparable to Western countries, at approximately 1% (Sun et al., 2019). The World Health Organization estimates that 0.76% of children worldwide have ASD, and the Chinese government has elevated the priority of this disease to the level of national scientific and technological strategic planning, making childhood ASD one of the major diseases of concern (Kou et al., 2023).

As a gastrointestinal disease, inflammatory bowel disease (IBD) is a chronic nonspecific intestinal inflammatory condition of unknown etiology, comprising two main subtypes: Crohn's disease and ulcerative colitis (Hu & Pang, 2022). Recent studies indicate that in addition to core symptoms, nearly half of patients with ASD also develop IBD (Holingue et al., 2018). IBD is characterized by chronic inflammation of the gastrointestinal tract, with symptoms including abdominal pain, diarrhea, bleeding, and weight loss, as well as severe complications such as intestinal strictures or perforation requiring surgery (Kim et al., 2022). Children represent a high-risk population for IBD. In recent years, with advances in diagnostic technology, the detection rate of pediatric IBD has gradually increased, and the incidence of pediatric IBD in China shows an upward trend, seriously affecting the growth, development, and quality of life of affected children, thus warranting sufficient attention (Lin et al., 2020). Over 20% of IBD patients develop the disease during childhood, and IBD can affect children's physical and mental health, increasing the risk of developing ASD (Abramson et al., 2010).

2. Close Relationship Between Pediatric IBD and ASD

In recent years, the prevalence of IBD has been continuously rising, with increasing risk of diagnosing ASD among IBD patients, while nearly half of ASD patients are also diagnosed with IBD (Holingue et al., 2018), prompting deep consideration among many researchers. As a chronic nonspecific intestinal inflammatory disease of unknown etiology, IBD's influencing factors include genetics, environment, immunity, and gut microbiota, mainly comprising Crohn's disease and ulcerative colitis. Clinical manifestations such as abdominal pain, diarrhea, and hematochezia can affect the development of the nervous system in young children and subsequently impact cognition and emotion, exacerbating ASD-related symptoms to varying degrees (Zhu et al., 2022). However, there is currently no definitive conclusion regarding the relationship between childhood ASD and IBD, and in-depth exploration and analysis of their relationship will contribute to early diagnosis of ASD and the discovery of treatment strategies.

2.1 Correlation Analysis Between Pediatric IBD and ASD

Regarding the issue of IBD symptoms in patients with ASD, multiple studies have explored this topic. Some researchers conducted a systematic review and meta-analysis using eight observational datasets, ultimately confirming that individuals with ASD are more likely to develop IBD, ulcerative colitis, or Crohn's disease. In their primary analysis, assuming a temporal sequence from ASD diagnosis to IBD diagnosis, they found that patients with ASD have a 1.66-fold increased risk of being diagnosed with IBD later in life, meaning that patients with ASD are more likely to develop IBD than normal controls. In a secondary analysis, regardless of diagnostic order, the association between ASD and IBD was positive, and this association remained statistically significant when limited to ulcerative colitis or Crohn's disease (Kim et al., 2022). Other researchers conducted a retrospective prevalence study using a distributed query system across three general hospitals and one pediatric hospital. The study included over 14,381 patients with ASD as samples and characterized their comorbidities, measuring the prevalence of these comorbidities in ASD. The results showed that the prevalence of IBD in individuals with ASD was 0.8%, and the prevalence of IBD increased with the age of children with ASD (Kohane et al., 2012). In a retrospective case-cohort study using records from the Military Health System database, researchers found that the prevalence of Crohn's disease and ulcerative colitis was higher in children with ASD than in control groups, also confirming the association between ASD and IBD (Lee et al., 2018). These findings demonstrate that the risk of IBD is significantly elevated in patients with ASD.

Regarding the possibility of diagnosing ASD in patients with IBD, numerous researchers have investigated this question. Butwicka et al. employed a cohort study methodology to analyze data from Swedish national healthcare and population registers, examining 6,464 individuals diagnosed with childhood-onset IBD (3,228 with ulcerative colitis, 2,536 with Crohn's disease, and 700 with un-

classified IBD). The results indicated that among IBD patients, the risk of developing ASD increased by 40% (Butwicka et al., 2019). Doshi-Velez et al. further measured the prevalence of IBD in patients with ASD, assessing IBD incidence among individuals with and without ASD across a medical benefits company, two pediatric tertiary care centers, and a national ASD repository. They ultimately found that the prevalence of IBD in patients with ASD was higher than in their respective control groups, with an overall significant difference, demonstrating the link between IBD and ASD (Doshi-Velez et al., 2015). Compared with the general population, individuals with IBD appear to have higher odds of developing schizophrenia, ASD, and dementia (Fousekis et al, 2021). Chinese scholar Chen Tao retrospectively analyzed clinical data from 294 patients diagnosed with IBD, 155 with Crohn's disease, and 129 with ulcerative colitis between March 2013 and May 2018, matching them with 1,176 normal controls. The study concluded that there is a certain association between IBD and ASD, with IBD patients having a greater probability of developing ASD compared to the normal population (Chen, 2018). These research findings collectively suggest that the risk of ASD is significantly elevated in patients with IBD.

In summary, whether analyzing the risk of ASD in IBD patients or the risk of IBD in ASD patients, different studies have demonstrated that patients with either disease have a significantly increased risk of developing the other disease, indicating a significant association between IBD and ASD. However, analysis of existing studies shows that the risk of developing IBD in patients with ASD increased by 1.66-fold (Kim et al., 2022), whereas the risk of developing ASD in patients with IBD increased by 40% (Butwicka et al., 2019). This suggests that the probability of detecting IBD in patients with ASD is higher, while the probability of diagnosing ASD in patients with IBD is relatively lower, hinting that the impact of ASD on IBD may be stronger. However, due to differences in sample sizes and diagnostic criteria, this conclusion requires further research for confirmation.

2.2 Genetic Correlation Between Pediatric IBD and ASD

Early studies have demonstrated that ASD has genetic correlations. Researchers utilizing twin studies for ASD heritability analysis have shown that ASD has strong genetic correlations (with estimates around 91%) (Tick et al., 2016). A previous study on familial risk of ASD estimated its heritability at 83%, suggesting that genetic factors may explain most of the risk for ASD, and that ASD risk increases with genetic relatedness (Sandin et al., 2017). Similarly, IBD also exhibits genetic correlations. Research indicates that the occurrence of IBD not only shows racial differences but also demonstrates familial clustering, with its incidence being 10%~20% higher in individuals with a family history compared to those without (Li et al., 2008). A twin study also demonstrated genetic correlations in IBD risk, with a magnitude higher than that for Crohn's disease and ulcerative colitis (Gordon et al., 2015). Although both ASD and IBD have their respective genetic correlations, Sadik et al. employed linkage disequilib-

rium score regression, a method that allows estimation of genetic correlations between complex traits IBD and ASD through genome-wide association summary statistics (B. Bulik-Sullivan et al., 2015; B. K. Bulik-Sullivan et al., 2015). Ultimately, there is no clear evidence indicating genetic correlations between ASD and IBD, ulcerative colitis, or Crohn's disease, meaning that IBD and ASD do not have genetic correlations (Sadik et al., 2022).

Several possible reasons may explain why genetic correlations have not yet been demonstrated between IBD and ASD: First, genetic defects in IBD and ASD can be either inherited from parents or result from de novo mutations. De novo mutations refer to situations where parents have normal genetic material, but the child's genetic material mutates, causing disease. Current research primarily conducts statistical analysis through cases of dominant inheritance, thus the conclusion of non-correlation requires further confirmation. Second, incomplete penetrance of IBD and ASD may also lead to biased experimental results. During inheritance, parents may carry genetic defects for IBD and ASD without manifesting symptoms, while these defects become apparent in their children. Finally, the occurrence of IBD and ASD is not solely influenced by genetic background; environmental factors also play important roles. Future research could consider investigating genetic correlations between the two conditions from the perspective of expressed and non-expressed genes, hoping to provide assistance for early screening and prevention of childhood ASD.

2.3 Causal Relationship Between IBD Genetic Susceptibility and ASD

Since increasing evidence supports an association between IBD and ASD, does a causal relationship exist between IBD and ASD? Addressing this question, some researchers have explored the causal relationship between the two conditions. They employed genome-wide association summary data for two-sample Mendelian randomization analysis to investigate the causal relationship between IBD and ASD, as well as the reverse causal relationship between ASD and IBD. The results indicated that genetic susceptibility to IBD is significantly associated with increased ASD risk, with genetic susceptibility to both Crohn's disease and ulcerative colitis significantly increasing the risk of developing ASD, establishing a causal relationship between IBD genetic susceptibility and ASD. However, genetic susceptibility to ASD does not have a causal relationship with IBD, meaning that the reverse causal relationship does not hold (Zeng et al., 2022).

Sadik et al. employed the same research methodology, extracting common genetic variants closely associated with Crohn's disease and ulcerative colitis and evaluating their causal effects on 18,381 ASD cases and 27,969 control samples. Their analysis results indicated that genetic susceptibility to ulcerative colitis has a causal relationship with ASD, and genetic susceptibility to Crohn's disease also has a causal relationship with ASD, though with weaker significance. Meanwhile, reverse causality assessment did not find any causal effect of ASD genetic susceptibility on either condition. These two studies yielded consistent

results: IBD genetic susceptibility has a causal relationship with ASD, but the reverse causal relationship between ASD and IBD genetic susceptibility does not hold (Sadik et al., 2022).

In summary, research indicates that an association exists between IBD and ASD, and that this is a causal relationship, but the reverse causal relationship between ASD and IBD has not been confirmed in current studies. This suggests that IBD may be one of the causes of ASD, while ASD may not be a significant factor among the many causes of IBD. Future research could further explore the causal relationship between IBD and ASD through richer sample resources, stricter diagnostic criteria, and more reasonable study designs, providing data support for clarifying the etiology of ASD and developing effective clinical intervention strategies.

3. Relationship Between Parental IBD and Childhood ASD

After clarifying the relationship between IBD and ASD in patients themselves, some researchers have proposed that parental IBD can lead to a series of adverse factors during pregnancy and the perinatal period, such as immune dysregulation, altered intestinal microenvironment, micronutrient malabsorption, and anemia (Tan et al., 2020; Wiegersma et al., 2019). Previous reports have indicated that diabetes and anemia can induce chronic inflammation, leading to increased inflammatory cytokines such as interleukins that can cross the placenta, affect fetal brain development, and potentially cause ASD (Krakowiak et al., 2012; Wiegersma et al., 2019). However, there is currently no definitive conclusion regarding the relationship between parental IBD and childhood ASD, and the underlying etiology of any association remains unclear, making the relationship between parental IBD and childhood ASD a question worthy of further investigation.

Sadik et al. conducted a nationwide population-based cohort study using Swedish registers to investigate the relationship between parental IBD diagnosis and childhood ASD. Using a sample of 2,324,227 children born to 1,282,494 mothers and 1,285,719 fathers, they performed logistic regression analysis and established three models to assess the association between parental IBD diagnosis and childhood ASD. The results indicated that maternal IBD diagnosis was associated with childhood ASD, with similar results observed in analyses of maternal ulcerative colitis and Crohn's disease diagnoses and childhood ASD, though the association between paternal IBD and ASD was weaker than the maternal association (Sadik et al., 2022). Other studies have shown that fetal exposure to an inflammatory maternal environment may increase the risk of ASD, and that offspring of maternal immune activation exhibit symptoms such as social impairments and repetitive behaviors (Wu et al., 2018). Another study suggested that maternal autoimmune disease is associated with increased risk of childhood ASD (Han et al., 2021). In contrast to these studies, Lee et al.'s results indicated that only paternal IBD was associated with increased likelihood of ASD in offspring, finding no association

between any maternal autoimmune diseases and offspring ASD risk (Lee et al., 2021).

Prior to these studies, many researchers had conducted detailed explorations with considerably different results. Atladottir et al. examined a sample of 689,196 children born in Denmark, among whom 3,325 children were diagnosed with ASD and 1,089 with infantile ASD. They ultimately found no increased risk of infantile ASD in children with siblings or parents with Crohn's disease or ulcerative colitis, meaning no statistically significant association was found between parental IBD and ASD or infantile ASD (Atladottir et al., 2009). Subsequently, researchers conducted a nationwide cohort study in Denmark with a sample of 1,005,330 children, among whom 11,888 (1.2%) had parents with IBD, and 8,087 (0.8%) were diagnosed with ASD during up to 17 years of follow-up. Over ten years, the risk of ASD in children with parental IBD was 0.7%, compared to 0.9% in children without parental IBD. They did not find an increased risk of ASD in children with parental IBD, and the same results were observed for Crohn's disease and ulcerative colitis. The overall results of this study indicated no significant association between parental IBD and offspring ASD risk (Andersen et al., 2014).

The contradictory results between earlier and later studies may be attributed to the following reasons: First, the age stages of ASD patients included in different studies varied, with researchers selecting ASD patients of different ages, which may lead to differences in diagnostic criteria for ASD symptoms across age stages, ultimately affecting experimental results. Second, diagnostic technologies for IBD and ASD also influence experimental results. With continuous advances in medical standards, the diagnostic accuracy for IBD and ASD has continuously improved, potentially causing deviations between more recent and earlier results. Finally, different statistical analysis methods used by researchers may also contribute to divergent results. Therefore, future in-depth investigations into the relationship between parental IBD and childhood ASD should consider factors that may cause experimental bias and control for them. More empirical studies are also needed to explore the association between parental IBD and childhood ASD, providing reference for investigating the etiology and early prevention of childhood ASD.

4. Treatment Methods for IBD and ASD

Numerous studies have demonstrated that IBD is significantly associated with childhood ASD. A Swedish national cohort study indicated that IBD patients have a significantly increased risk of developing ASD (Butwicka et al., 2019). Researchers using two-sample Mendelian randomization design have also found a causal relationship between IBD and ASD, but no reverse causal relationship between ASD and IBD (Zeng et al., 2022). The more severe the IBD, the more likely ASD symptoms are to appear, providing a new approach for early screening and intervention of ASD symptoms. Researchers have begun investigating strategies to prevent or alleviate ASD-related symptoms through IBD

treatment, aiming to improve patients' psychological status and quality of life. Currently, biologic therapy, antibiotics, and fecal microbiota transplantation are commonly used treatments for IBD and ASD. Prognosis and alleviation of IBD through these methods may help reduce the occurrence of ASD symptoms in IBD patients. Certainly, further research can be conducted in the future to explore more clinical strategies for intervening in ASD through IBD treatment.

4.1 Biologic Therapy

As the number of IBD patients continues to increase, treatment methods for IBD and ASD are constantly being improved. In recent years, biologics have made continuous breakthroughs in research and development, with significant clinical treatment effects. The importance of biologics in IBD treatment has gradually become apparent, and they have become the preferred treatment option recommended by domestic and international guidelines (Feuerstein et al., 2020; Wu et al., 2018). Currently, four biologics are approved for IBD treatment in China, including infliximab, adalimumab, ustekinumab, and vedolizumab (Liu et al., 2022), and newer agents such as ustekinumab and vedolizumab have shown good efficacy in treating patients who have lost response to other therapies (Yang et al., 2022).

The medications used to treat IBD differ between patients with and without ASD. Investigators have found that IBD patients with ASD are more likely to receive biologics such as adalimumab and certolizumab, with higher utilization rates for these two agents. They are commonly used for treating moderate to severe IBD patients and can effectively treat IBD and intervene in the emergence of ASD symptoms (Lee et al., 2018). Similarly, vedolizumab, as a gut-selective monoclonal antibody, can specifically bind to integrin $ 4 $7, inhibiting T lymphocyte migration to the intestine, thereby achieving remission of IBD (including ulcerative colitis and Crohn's disease) (Liu et al., 2022). Suppression of IBD can substantially improve patients' mental health status and play a certain role in ASD prevention. Although biologics have already shown significant effects in treating IBD, their efficacy in intervening and alleviating ASD symptoms requires further clinical practice, meaning more actual cases are needed to further confirm that treating IBD with biologics can play a role in preventing ASD.

4.2 Antibiotics

Following nutritional supplement therapy, restricted or special diets, hyperbaric oxygen therapy, intravenous immunoglobulin therapy, and other treatments, antibiotics have begun to be used for treating intestinal symptoms, and this method has also been helpful for ASD treatment. Some ASD patients have shown therapeutic effects after oral administration of vancomycin and metronidazole, two antibiotics widely used for anaerobic bacterial infections (Duan et al., 2015). Other studies have found that after eight weeks of vancomycin treatment, patients showed improvements in task performance, compliance with parental requests, environmental awareness, and persistence in engaging in pos-

itive activities, with significant reductions in repetitive and self-stimulatory behaviors (Sandler et al., 2000). Vancomycin may primarily exert its effects by influencing Gram-positive anaerobic bacteria, and high concentrations of vancomycin also eliminate *Clostridium difficile* and most Gram-negative anaerobic bacteria, thereby treating IBD problems in patients (Sandler et al., 2000).

Oral vancomycin or combined use with gentamicin has shown efficacy in children with refractory very early-onset IBD (Lev-Tzion et al., 2017). However, vancomycin and gentamicin are typically reserved for severe diseases when other antibiotics are ineffective and are considered the last line of defense against resistant bacteria. Once misused, they can easily cause bacterial resistance, so such antibiotics should be selected with caution in ASD treatment (Duan et al., 2015). Additionally, the therapeutic effective period of vancomycin for ASD is relatively short, and ASD symptoms may recur once the medication is discontinued. Future research should continue to explore drugs with longer therapeutic durations to achieve sustained alleviation of IBD and ASD symptoms.

4.3 Fecal Microbiota Transplantation

Fecal microbiota transplantation (FMT) is an emerging IBD treatment method that involves implanting feces from healthy individuals into the intestines of IBD patients to reconstruct a normal gut microbiome environment. It can be used to treat gastrointestinal and other types of diseases, with its mechanism achieved through restoring gut microbiota and controlling the intestinal immune system (Niu et al., 2022). As a therapeutic approach, FMT is not only used for treating human gastrointestinal diseases such as IBD, irritable bowel syndrome, metabolic syndrome, and autoimmune enteropathy (Duan et al., 2015), but may also have certain efficacy for psychiatric conditions like Parkinson's disease and childhood ASD (Jiang et al., 2014). FMT treatment is associated with significant improvement in ASD symptoms such as social impairments and repetitive behaviors (Kang et al., 2019) and with disease remission in ulcerative colitis patients (Moayyedi et al., 2015). Transplanting gut microbiota from ASD patients into germ-free mice leads to the emergence of ASD symptoms (Sharon et al., 2019), while treating mouse models with ASD characteristics using human commensal bacteria alters microbial composition and improves deficits in communication, stereotypy, anxiety, and sensorimotor behaviors (Hsiao et al., 2013).

However, FMT may have immediate adverse reactions such as abdominal bloating, diarrhea, constipation, vomiting, and transient fever, and may also lead to diseases associated with gut microbiota changes, including obesity, diabetes, colon cancer, and asthma (Zou & Zheng, 2020). The composition of standardized human gut microbiota used in FMT research depends largely on donor conditions. To improve FMT efficacy and ameliorate ASD-related symptoms and behavioral manifestations, further research is needed to identify bacterial species that play a decisive role in donor standardization (Ye et al., 2020). Future research could further investigate the long-term efficacy and safety of FMT

for treating IBD and ASD to identify safer, more effective, and more economical FMT approaches.

5. Summary and Outlook

Through summarizing and analyzing research literature on the relationship between IBD and ASD, we have gained further understanding of their association. Children with IBD have a higher risk of developing ASD than children without IBD. Similarly, among children with ASD, the risk of being diagnosed with IBD is also significantly elevated, indicating a significant correlation between pediatric IBD and ASD. Additionally, IBD has a causal relationship with ASD, but ASD does not have a reverse causal relationship with IBD. Analysis of the relationship between parental IBD and childhood ASD shows that parental, especially maternal, IBD is associated with childhood ASD. However, current empirical research literature on the causal relationship between IBD and ASD remains insufficient, requiring more empirical studies for further confirmation and refinement. Finally, several IBD therapies have been summarized that can effectively alleviate ASD-related symptoms, which may be promoted for wider clinical use in the future.

Future research on the relationship between IBD and ASD may face the following issues: First, the existence of a causal relationship from ASD to IBD but not the reverse requires more empirical evidence for verification. During research, sample size, age, diagnostic criteria for ASD and IBD, disease severity, and analytical models used can all influence experimental conclusions. Therefore, in confirming forward and reverse causality, influencing factors should be kept as consistent as possible to obtain more convincing conclusions. Second, proving genetic correlations between IBD and ASD presents considerable difficulty. This involves the influence of dominant and recessive inheritance, and judgment based solely on dominant results may not comprehensively explain the issue, leading to conclusions of non-correlation. Thus, future investigations of genetic correlations should simultaneously consider the roles of dominant genes, recessive genes, and environmental factors. Third, although previous studies have demonstrated correlations between ASD and IBD, the pathophysiological mechanisms of the two conditions remain unclear. Subsequent research could consider exploring the pathogenic mechanisms and common influencing factors of both conditions through bioinformatics tools to analyze potential regulatory factors. Fourth, determining whether a causal relationship exists between parental IBD and childhood ASD is difficult. Due to inconsistent findings in existing studies, more robust research is needed to prove the relationship between the two. In exploring this relationship, both paternal and maternal factors must be considered, while controlling for or excluding interference from other factors that may cause childhood ASD, with strict standards in sample selection and classification. Fifth, investigations into childhood ASD and IBD may lack clinical diagnosis of IBD symptoms by physicians. For children with ASD, especially those with language impairments or intellectual disabilities, researchers

may use parent-reported symptoms during data collection, and such symptom reports are susceptible to bias influenced by the ASD diagnosis. Therefore, future research may require more objective assessment of IBD symptoms through clinical diagnosis.

Addressing the limitations of current research on the relationship between IBD and ASD, several elements require further attention in future investigations: First, attention should be paid to sample data sources in the research process. Current studies mostly select samples from European and American ancestry, such as from Sweden, Denmark, and the United States, with very few samples from Asian ancestry, which may involve sample racial selection bias in experimental procedures. Second, consider quantifying the severity of IBD and ASD. Currently, there are no detailed studies on the relationship between different IBD severity levels and ASD. Future research could consider adopting more advanced data collection or analysis methods to quantify the severity of both diseases. Quantification of severity would provide stronger evidence for research and increase the clinical significance of association studies. Third, find suitable non-invasive methods for IBD screening. Early diagnosis of IBD is very important and necessary, but there is currently a lack of guidelines emphasizing the necessity of early IBD screening and treatment in ASD patients. If guidelines for non-invasive detection for early IBD screening and monitoring of gastrointestinal symptoms in ASD patients can be established in the future, it would greatly assist in the treatment of IBD and ASD. Fourth, consider using multiple combined approaches for ASD screening or diagnosis. For example, ASD could be screened through detection of inflammatory factors, and genetic testing could also be considered for diagnosis. Identifying common genetic loci between IBD and childhood ASD and targeting them for intervention may provide help for clinical treatment.

Currently, the main strategy for patients with both IBD and ASD, or for patients with IBD who need to prevent later ASD symptoms, is to achieve ASD alleviation or prevention through IBD treatment. Commonly used methods include biologics, antibiotics, and fecal microbiota transplantation. However, antibiotics may produce significant side effects, easily cause gut microbiota dysbiosis, and even generate drug resistance. Their therapeutic effects on IBD and ASD are relatively short-lived, with recurrence risks once medication is stopped. In contrast, biologics and fecal microbiota transplantation, while also having some transient adverse reactions, have better and more durable therapeutic effects on ASD symptoms in IBD patients. These two methods could be considered as priority treatment options, but more clinical practice is needed to investigate their safety and cost-effectiveness. During treatment, the durability and cost-effectiveness of therapeutic effects should be considered, attempting to adopt combined strategies of multiple treatment methods, such as combining basic drug therapy with nutritional therapy, biologics treatment, and behavioral or psychological interventions, to identify the most effective methods for alleviating ASD-related symptoms through IBD treatment.

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Note: Figure translations are in progress. See original paper for figures.