Introduction

Autism Spectrum Disorder (ASD) is a multifaceted neurodevelopmental condition that impacts various aspects of typical mental development. It encompasses a broad range of challenges, spanning from language and communication difficulties to repetitive behaviors, as well as disruptions in motor skills and sensory processing. One of the key elements contributing to the development of ASD is a significant genetic influence: established research has indicated that the heritability of ASD ranges from 60% to over 80%. The genetic factors contributing to ASD are remarkably diverse, with only a limited number of genes that have been extensively studied and associated with the disorder. Food restriction, selective eating habits, and gastrointestinal (GI) disorders are prevalent medical conditions associated with ASD. Autistic children often exhibit picky eating behaviors, with aversions to specific food characteristics such as color, texture, and odor, which can negatively impact their diet quality and nutrition. In addition, immune dysfunction, increased intestinal permeability, microbiota imbalances, and gut infections have been observed in many autistic children and GI inflammation and discomfort is common in autistic individuals. Overall, the prevalence of gastrointestinal symptoms in autistic individuals is nearly two times higher than that of typical children, with ranges between 0% and 69% (Lasheras et. al, 2023) in one study, and 55% in another (Gan et. al, 2023).

Because of these underpinnings, a significant research question arises: what causes the correlation between gastrointestinal distress and autism? Understanding the factors underlying this association is crucial in unraveling the complexities of ASD and developing effective interventions and appropriate treatments. This paper will aim to synthesize existing research into three potential causes for consideration: behavioral factors such as food avoidance and stress, biological factors such as gut microbiota and environmental contributions, and inherited or genetic factors.

Criteria

This review's inclusion criteria encompasses a range of research designs, including observational prospective and retrospective studies, case-control studies, cohort studies, and systematic reviews. These studies must focus on one or more of the following topics: autistic individuals who presented gastrointestinal symptoms, examination of the correlation between genes and gastrointestinal symptoms or disease in autistic individuals, or the exploration of the dietary and behavioral factors that might influence observed gastrointestinal symptoms or disease in autistic individuals. All studies falling within the timeframe of the past two decades were considered, and studies were selected based on novelty, recency, and relevancy to the research topic. Finally, to insure the quality and reliability of the research, my inclusion was limited to studies that had undergone peer review and were published in reputable journals, with contributing authors that have an advanced degree of study in fields such as psychology, psychiatry, genetics, gut microbiology, dietary science, and/or the gastrointestinal system. In addition to research that does not qualify for exclusion, I have excluded animal models and other model studies, as well as letters, notes and conference abstracts, online forums and anecdotal boards, and articles with lack of specific data.

Behavioral Factors

There is strong evidence of a correlation between psychiatric comorbidities and GI symptoms, ranging from increased intestinal permeability to stomach cramps. Many studies exist that explore this relationship in comparison to neurotypical people, “the odds ratio for children with ASD with at least one GI symptom was 3.64:1,” (Gan et. al, 2023) but the relationship may go deeper for autistic individuals with additional psychiatric comorbidities. In a study around the psychological, behavioral and biological factors associated with GI symptoms in autistic adults, “GI symptoms were strongly associated with psychiatric comorbidity (anxiety and/or depressive disorder), increased perceived psychological stress levels and worse perceived health,” (Warreman et. al), which indicates that one’s perception or outlook of health, in addition to other psychological stress factors, may directly impact gastrointestinal function. In addition to psychiatric comorbidities, an individual’s coping mechanisms may come into play. In a study conducted on the statistical significance of correlations between intelligence, autism, GI disease, and other psychiatric comorbidities, avoidant coping exhibited a high correlation with combined conditions, followed by emotion-focused coping; however, problem-focused coping strategies correlated with a lower rate of reported conditions (Fries et. al, 2022). The strong correlation between psychiatric comorbidities and gastrointestinal symptoms in autistic individuals is well-documented, with increased risk ratios and associations with perceived psychological stress levels and overall perception of health. However, more research ought to be conducted to explore whether the psychiatric comorbidities are a correlation with or without a common cause, or a potential cause for the gastrointestinal distress. Additionally, the coping strategies employed by autistic individuals may play a significant role in these complex relationships, which suggests the potential to control at least some of the symptoms through mental health interventions.

Dietary choices are another perspective to consider when examining behavioral factors that influence autistic individuals’ digestive health. However, the relationship between diet, GI symptoms, and behavioral factors in autistic individuals is complex and not fully understood. Up to 41.6% of autistic individuals display mild selective eating habits, while 26% have severe picky eating, compared to 32.9% and 11%, respectively, for neurotypical individuals (Gan et. al, 2023). This behavior can be in part related to sensitivities to food taste, texture, smell, or appearance, or to an increased rate of resistance to new foods (Bresciani et. al; Gan et. al, 2023). Food selectivity can lead to a limited and unbalanced diet, which can in turn lead to impacted gut microflora and an increased prevalence of gastrointestinal distress. In fact, one study found “altered taxonomic (gut microbiologic) diversity in ASD significantly correlated with autistic symptoms, thought problems, delinquent behaviors, self dysregulation, and somatic complaints,” (Chen et. al, 2022) and several studies explored dietary interventions in autistic individuals to impact gut-related symptoms and gut microflora with inconclusive results.

Biological Factors

There is an intricate relationship between ASD and gastrointestinal physiology, where diet and GI abnormalities show strong correlations with gut microbiota and behavior. According to Ristori et. al, strong food selectivity deeply affects gut microbiota composition, and autistic patients appear to have elevated levels of short-chain fatty acids (resulting from non-digested carbohydrates) “in the stool and serum, and increased level of SCFA-producing bacteria,” (Ristori et. al, 2019). Furthermore, the presence of certain gut bacteria can result in changes in serotonin levels and inflammatory responses, affecting both GI symptoms and neurodevelopmental aspects (Ristori et. al, 2019). In a meta-analysis that reviewed these relationships, children with ASD and their corresponding gut bacterial anomalies varied regionally, with rates of Bacteroides in “Asia (31.44%) was significantly higher than that in America (20.47%) and Europe (9.05%),” suggesting that regional differences in diet, living habits, and consumption levels has a “huge impact on the intestinal microbes of people in the region,” (Gan et. al, 2023). While this research highlights significant correlations in dietary variations and manifestations of symptoms, it is unclear how extensive the impact of diet is compared to genetics, stress, and other variables. Furthermore, research has examined the impact of intentional dietary practices on autistic individuals’ gastrointestinal health, where “patients with autism on a reported gluten-casein-free diet had significantly lower IPT values compared with those who were on an unrestricted diet and controls” (de Magistris et. al, 2010). Food selectivity, regional variations, and intentional dietary practices may all contribute to the gastrointestinal health of autistic individuals.

The impact of gut microflora on autism and gastrointestinal symptoms is complex and research is ongoing. In a study on the influence of gut microbiota and behavioral problems in autistic patients, experts found that autistic individuals with reported GI symptoms had higher levels of certain bacteria like Fusobacterium, Ruminococcus, and Bacteroides plebeius, with lower levels of Ruminococcaceae and Turicibacter, but while these alterations in gut environment correlate with GI symptoms, they may not directly impact GI symptoms (Chen et. al, 2022). While this information appears to imply that these bacteria have a direct impact on gastrointestinal distress, “the function of the identified microbial profiles mainly involves the immune pathway,” (Chen et. al, 2022) which implies that the GI symptoms may be caused instead by immune dysregulation. This is supported in a separate study on gut microbiota ecology and inferred functions in children by Vernocchi et. al, 2022, where the study’s findings reveal that autistic children showed lower levels of secretory immunoglobulin A (sigA) in their stool samples compared to control subjects, suggesting compromised gut immunity. In a Dutch Lifelines Study, other biological variables such as BMI and waist circumference were not associated with GI symptoms, but in both the ASD and control groups, “GI symptoms were positively associated with total leukocyte, lymphocyte and neutrophil counts,” (Warrenman et. al, 2023) which strengthens the probability that gut microflora may impact both the psychological and immunological factors of autistic individuals. This raises the question of whether the cause for these co-occurrences could be impacted by the immune system through genetic or environmental dysregulation.

Inherited Factors

Research has shown that there is a hereditary component to ASD, and some of these genetic factors may also influence the risk of experiencing gastrointestinal issues. Over 152 genes have been identified as “risk genes” for ASD (Cirnigliaro et. al, 2023) while at least 49 genes are identified as risk genes for diverticular dysfunction (Camilleri et. al, 2020) without the discussion of potential genetic overlap. In both Cirnigliaro et. al and Camilleri et. al, FBXL13 was identified as a risk gene for ASD and Diverticular Disease, respectively, but has not yet been studied as a risk factor for simultaneous comorbidity. However, it is clear that the gut and the brain share some common genetic pathways, and disruptions in these pathways could affect both neurological and gastrointestinal function. In another study, a total of 98 common genes were identified by weighted gene coexpression network analysis, with a total of seven genes and four hub genes that linked to both ASD and Inflammatory Bowel Disease with differing potential interactions “Among them, the ferroptosis-related gene NCOA4 and the immune-related gene TLR4 (toll-like receptor 4) were significantly positively correlated with hub genes in both diseases” (Zhu et. al, 2023). While many genes have been identified as risk factors, this overlap remains an understudied territory, and evidence suggests that shared genetic pathways underpinning neurological and gastrointestinal functions could hold the key to understanding the co-occurrence and potential treatment of these conditions.

In addition to genetic study, reporting on family traits and health may shed additional light on potential inherited causes of these comorbidities. In a study on maternal health during pregnancy, factors such as weight, blood pressure, and respiratory wellness showed a statistical significance in the increased likelihood of ASD and gastrointestinal disturbances in offspring. These children “had the largest proportions of nulliparous mothers” with “histories of comorbidities” compared to neurotypical children, and of the maternal health considerations studied, “the highest proportions of maternal obesity, diabetes mellitus, preeclampsia, and asthma diagnoses were observed in children diagnosed with ASD and GIDs,” (Carter et. al, 2023). In a separate study on intestinal barrier permeability for autistic individuals and their first-degree relatives, “a high percentage of abnormal IPT values were found among patients with autism (36.7%) and their relatives (21.2%) compared with normal subjects (4.8%),” which suggests a strong case for inherited traits that influence intestinal permeability in autistic patients (de Magistris et. al, 2010). This information suggests that both genetic and maternal factors play a role in the comorbidities of ASD and gastrointestinal disturbances.

Conclusion

The information presented reveals a complex interplay of behavioral, biological, and inherited factors in the co-occurrence of Autism Spectrum Disorder and gastrointestinal distress. Behavioral factors, including psychiatric comorbidities, dietary choices and selectivity, and coping mechanisms, strongly influence reported gastrointestinal symptoms in autistic individuals, and may affect gut microbiota. Biological factors, on the other hand, show correlations between gut microbiota, immune

dysregulation, and potential effects on gastrointestinal health and psychological well-being. Finally, inherited factors, including genetic risk genes and maternal health during pregnancy, may also play a role in the comorbidities of autism and gastrointestinal distress. These overlaps hold promise for understanding and potential interventions in these conditions, but more research needs to be conducted to understand which factors are cause and which are effect.

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