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Autism Spectrum Disorder and Eating Problems: The Imbalance of Gut Microbiota and the Gut-Brain Axis Hypothesis

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This review explores the complexities of autism spectrum disorder (ASD), primarily focusing on the significant eating challenges faced by children and adolescents with this neurodevelopmental condition. It is common for individuals with ASD to exhibit heightened sensitivity to various sensory aspects of food such as taste, texture, smell, and visual appeal, leading to restricted and less diverse diets. These dietary limitations are believed to contribute to an imbalance in the gut microbiota. This review elaborates on how these eating problems, coupled with the distinctive characteristics of ASD, might be influenced by and, in turn, influence the gut-brain axis, a bidirectional communication system between the gastrointestinal tract and the brain. This discussion aims to shed light on the multifaceted interactions and potential implications of diet, gut health, and neurological development and function in children and adolescents with ASD.

Keywords: Autism spectrum disorder; Eating disorder; Gastrointestinal tract; Microbiome; Gut-brain axis.

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INTRODUCTION

Autism spectrum disorder (ASD) is a developmental disorder marked by impairments in social interactions and communication skills, coupled with repetitive behaviors and restricted interests [1]. Many children and adolescents diagnosed with ASD experience significant eating challenges [2]. Many factors contribute to these dietary challenges, including enhanced sensitivity to the sensory qualities of food such as taste, texture, smell, and appearance [2]. Furthermore, individuals with ASD frequently find it difficult to incorporate new foods into their diet or adapt to various eating methods [2]. Many individuals find articulating food preferences or dietary needs daunting, which commonly leads to anxiety related to mealtimes [2]. Children with ASD who display restricted interests tend to consume limited diets [3] indicating that restricted interest could induce an imbalance in the gut microbiota of children and adolescents with ASD.

ASD AND FOOD SELECTIVITY

Food selectivity is a prevalent eating challenge in ASD, exposing children to heightened risks of inadequate intake of vital minerals and vitamins, which impacts their developmental trajectory [4]. Furthermore, pronounced food selectivity in toddlers with ASD correlates with the intensification of autism symptoms [4].

Sensory sensitivity

Atypical sensory processing in ASD represents a crucial, albeit less frequently discussed, subject of discourse. This phenomenon is conspicuous across various sensory realms, including touch, smell, and taste, and manifests with greater prevalence in children with ASD than in those exhibiting other developmental disabilities or those with typical development [5]. The resultant sensory sensitivities often materialize as under-responsivity (diminished reactions to sensory stimuli), over-responsivity (amplified or adverse reactions to sensory stimuli), or a composite of both. These sensory idiosyncrasies are enduring, unaffected by age or ASD severity, can be discernible from early childhood, and persist throughout the individual's lifetime [5].

Sensitivity, specifically within the oral sensory domain, has pronounced implications for dietary behaviors. There is a link between food selectivity in ASD and sensory processing malfunctions with a specific focus on oral sensory sensitivity [4-8]. Children with distinctive oral sensory sensitivi-

ties exhibit broader rejection of food varieties and diminished intake of vegetables than those devoid of such sensitivities [9]. Conversely, a deficiency in taste sensitivity is associated with increased symptoms of eating disorders [4]. Moreover, enhanced sensitivity in the visual domain correlates with heightened symptoms of both eating disorders and ASD-specific eating habits [4].

An in-depth investigation into sensory sensitivities and their diverse implications for the dietary patterns of children and adolescents with ASD is vital, given the intricate relationship between sensory processing and dietary choices. A comprehensive understanding of their varied manifestations and the formulation of customized intervention strategies designed to accommodate the unique requirements of those navigating the complexities of the autism spectrum is required to effectively address these sensory peculiarities.

Neophobia

Food selectivity and neophobia manifest in children with ASD due to sensory sensitivity, adaptability issues, and anxiety [9]. A comprehensive review titled "*Food Selectivity and Neophobia in Children with Autism Spectrum Disorder and Neurotypical Development*" demonstrated that children with ASD are more predisposed to exhibit food selectivity and neophobia than their neurotypically developing peers [9]. This study highlighted the considerable impact of such behaviors on the health and well-being of children with ASD, indicating risks such as malnutrition, being overweight, social isolation, and difficulties in social participation [9]. Due to the substantial implications for the health, development, and social inclusion of individuals within the spectrum, the manifestations of food selectivity and neophobia in ASD require meticulous consideration. Recognizing the multifaceted roots of these phenomena is pivotal for formulating effective and holistic interventions tailored to the unique needs and challenges faced by children with ASD.

Restrictive behavior

Restrictive behavior is another common characteristic of ASD that can significantly affect food choices [4]. This behavior may manifest as a rigid adherence to specific routines or rituals, leading to a limited range of acceptable foods and a refusal to try new ones. Furthermore, children with ASD may exhibit avoidant/restrictive food intake disorder (ARFID), a newly recognized eating disorder characterized by a persistent pattern of food restriction that is often unrelated to other medical conditions or cultural norms [10]. ARFID can lead to severe nutritional deficiencies, dependence on oral supplements, and the need for enteral feeding [10].

The precise definition of "food selectivity" in the context of ASD remains a subject of debate. However, studies suggest that rigid adherence to routines and rituals, along with sensory sensitivity and neophobia, contributes to the development of food selectivity in patients with ASD. A comprehensive approach is required to address these restrictive behaviors, considering their underlying causes and implementing individualized interventions.

DIET QUALITY AND NUTRITIONAL STATUS

Preschoolers with ASD often encounter significant challenges during mealtime, hindering their intake of essential nutrients and increasing their risk of nutritional deficiencies [11]. A case-control study comparing mealtime behaviors between Chinese preschoolers with ASD and typically developing preschoolers in Hong Kong revealed that the ASD group exhibited a significantly higher likelihood of food refusal and unhealthy eating habits [11]. This was evident in their higher scores on the Brief Autism Mealtime Behavior Inventory food refusal domain and the Chinese Preschoolers' Eating Behavior Questionnaire food fussiness and eating habit domains [11]. Additionally, the ASD group was less responsive to external factors that influenced eating and was less inclined to eat independently [11].

There is a pervasive trend among children and adolescents with ASD to maintain a diet of inferior quality compared with national standard datasets as shown by a cross-sectional study [12]. This study highlighted notable disparities in diet quality, with ASD individuals exhibiting higher consumption of whole grains, fatty acids, added sugars, and refined grains and a lower intake of whole fruits, total vegetables, dairy, total protein foods, seafood, and plant proteins [12].

An extensive meta-analysis of the dietary patterns of children with ASD inferred that this population had a lower intake of proteins, calcium, phosphorus, selenium, vitamin D, thiamine, riboflavin, and vitamin B12 than typically developing children [13,14]. In contrast, they consumed an elevated level of polyunsaturated fatty acids and vitamin E [13,14]. Children with ASD also have lower omega-3 consumption than those without, necessitating cautious interpretation of these results because of the limited number of studies included in the analysis and high heterogeneity [13,14]. The findings also indicate deviations from the Dietary Reference Intake recommendations, with lower intakes of calcium, vitamin D, and dairy and higher intakes of protein, phosphorus, selenium, thiamine, riboflavin, and vitamin B12 than recommended [13,14].

There have been two reported cases of children with ASD becoming critically ill because of vitamin deficiencies [15].

In the first instance, the child suffered from thiamine deficiency, culminating in beriberi, which can induce heart complications, nerve damage, and other severe health issues [15]. Despite prompt vitamin supplementation, the patient experienced a cardiac arrest and developed serious neurological complications [15]. Another child displayed symptoms of scurvy resulting from vitamin C deficiency, manifesting as leg pain and a limping gait [15]. In this case, the administration of intravenous vitamin C and tube feeding led to a quick recovery [15]. The authors emphasized the existence of other reports of critically ill children with ASD due to thiamine deficiency and underscored the necessity of early interventions to prevent severe vitamin deficiencies arising from the observed high food selectivity in children with ASD [15]. This is a clear demonstration of the link between food selectivity and vitamin deficiency in children with ASD [15]. Case reports have provided compelling evidence supporting the hypothesis that selective eating in individuals with ASD can lead to vitamin deficiency [15]. The detailed descriptions of children's diets and the subsequent development of vitamin deficiencies underscore the importance of addressing selective eating behaviors in ASD to ensure adequate nutrition and overall health.

Children with ASD often exhibit lower vitamin D levels at birth than their non-ASD siblings likely due to a combination of genetic, environmental, and dietary factors and potentially influencing ASD development [16]. Therefore, lower vitamin D levels may be correlated with the severity of autism symptoms, emphasizing the imperative need for extensive research to clarify the relationship between vitamin D levels and ASD and develop novel treatments focusing on vitamin D levels [16].

ASD AND MICROBIOTA-GUT-BRAIN AXIS HYPOTHESIS

The gut maintains multifaceted interactions with the brain via diverse pathways. It utilizes neuroactive molecules and microbial metabolites, such as short-chain fatty acids and neurotransmitters produced by entities such as enteroendocrine cells, as chemical intermediaries [1]. These substances can modulate the central nervous system activity either directly by traversing the blood-brain barrier or indirectly by influencing components such as the vagus nerve and the mucosal immune response [1]. The gut microbiota, including *Bifidobacterium* and *Prevotella*, maintain chemical dialogues with the brain through compounds such as short-chain fatty acids and serotonin (5-hydroxytryptamine), which significantly affect mood, behavior, and cognition by modulating the production of neurotransmitters and interacting with various physiological components [1].

Emerging evidence suggests that the microbiota-gut-brain axis plays a crucial role in the development and progression of ASD, with children with ASD exhibiting variations in gut microbiota composition [3,17-23]. Alterations in the microbiota-gut-brain axis lead to dysbiosis of the gut microbiota, resulting in an imbalance in chemical signals and cytokines, which, in turn, heightens neuroinflammation in the brain in individuals with ASD [1]. Microglial activation and neurochemical dysregulation, including anomalies in glutamate, gamma-aminobutyric acid, serotonin, and oxytocin levels in the ASD brain, are correlated with disturbances in the gut microbiota [1]. A functional architecture along the gut-brain axis correlates with the heterogeneity of ASD phenotypes [24]. This architecture is characterized by ASD-associated amino acid, carbohydrate, and lipid profiles, which are predominantly encoded by microbial species belonging to the genera *Prevotella*, *Bifidobacterium*, *Desulfovibrio*, and *Bacteroides* [24]. Furthermore, this architecture correlates with changes in brain gene expression, restrictive dietary patterns, and proinflammatory cytokine profiles [24]. A strong association has been observed between temporal changes in the microbiome composition and ASD phenotypes [24].

There are associations between the intake of certain foods and the presence of certain bacteria in the gut microbiota [21]. For example, the consumption of dairy products is associated with higher levels of *Lactobacillus*, whereas the intake of cereals is associated with lower levels of *Roseburia* [21]. Children with ASD who are overweight or obese have been found to have lower levels of *Roseburia* and *Faecalibacterium prausnitzii* in their gut microbiota [21]. These bacteria produce beneficial fatty acids and other metabolites [21]. Therefore, dietary interventions may improve the gut and overall health of children with ASD. However, further research is required to develop and test specific dietary interventions for patients with ASD. Importantly, diet is just one of many elements that may influence the gut microbiome. Other factors, such as genetics, environment, and medications, may also play a role.

Specific instances of altered gut microbiota in ASD include a diminished presence of butyrate-producing bacteria such as *Ruminococcaceae*, *Eubacterium*, *Lachnospiraceae*, and *Erysipelotrichaceae* and decreased levels of gamma-aminobutyric acid-synthesizing microbiomes such as *Bacteroides*, *Lactobacillus*, and *Bifidobacterium* [1]. Such alterations highlight the promise of therapeutic interventions, such as probiotics and dietary adjustments, to improve the gut microbiota and consequently alleviate ASD symptoms.

Table 1. List of literatures covering ASD and eating problems

Eating problem	[2, 11, 25-30]
Sensory sensitivity	[5 ,6, 27, 31-33]
Food selectivity	[4-6, 9, 10, 30, 34-55]
Nutritional intake	[13, 14, 21, 56-62]
Diet quality	[11, 12, 29, 63, 64]
Nutritional status	[21, 57-60, 65-76]
Others	[2, 3, 6, 11, 15, 16, 19, 28, 42, 57, 61, 63, 66, 75, 77-86]

ASD, autism spectrum disorder

CONCLUSION

Despite the extensive research and literature on ASD and eating problems (Table 1), there remains a need for greater attention to the management of these conditions.

There is a multifaceted relationship between specific gut microbiota, the gut-brain axis, and ASD, suggesting that improving gut health can be pivotal in alleviating ASD symptoms, with dietary interventions standing out as promising therapeutic strategies. Progressive research has elucidated the intricate pathways and significant roles of specific gut microbiota and the brain in regulating multiple brain functions, offering potential advancements in the understanding and management of ASD and its associated conditions, thus reinforcing the significance of continuous exploration in this complex biological domain.

Availability of Data and Material

Data sharing is not applicable to this article, as no datasets were generated or analyzed during the study.

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

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