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Microbiome Relationship in Autism Spectrum Disorder (ASD): Subject Review

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Abstract. *Importance of gut microbiota during neurodevelopment has increased, as has the potential relationship between the gut microbiota and (ASD). Complex associations between gut microbiota and ASD are explored here, including significant pathways such as immune modulation, neurotransmitter control, and gut-brain axis signaling. Based on available data, individuals with ASD possess distinctive microbial signatures that are characterized by reduced diversity and altered abundance of specific bacterial species. Such modifications could be related to symptoms of the behavioral nature, neuroinflammatory, as well as gastrointestinal. ASD growth as well as severity could be influenced by the composition of microbiome, depending on genetic, nutrition, microbial exposure during the earliest phases, as well as antibiotic use. Additional therapies based on the microbiome that presented the potential to alleviate the symptoms related to ASD include the use of probiotics, prebiotics, diet modification, as well as fecal microbiota transplantation (FMT). Still, establishing the causal associations, standardizing the procedure of handling the patients, as well as solving the problem related to the manipulation of microbiome, are still challenging activities, though. Large-scale, long-term studies need to be the core agenda of subsequent research, so that specific microbial signatures associated with ASD will be clearly defined, as well as tailored therapies that address the microbiome will be developed. Understanding more about the role that the microbiota plays during ASD may open up the diagnosis as well as the therapy based on the entirely new concepts, something that will ultimately benefit the patients who possess the disorder.*

Keywords: *Autism Spectrum Disorder; Gut Microbiota; Microbial Signatures; Neurodevelopment; Probiotic Therapy.*

1. INTRODUCTION

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by persistent difficulties in social interaction and communication, along with restricted and repetitive patterns of behavior and interests (American Psychiatric Association, 2013). The connection between the digestive system and the brain(GBA), a two-way communication setup linking the brain with the stomach and intestines, has become a major point of focus in figuring out the biological reasons behind ASD. This system uses nerve signals, hormones, and immune system signaling methods (Cryan *et al*., 2023). More and more information shows that changes in the types of bacteria in the gut, often called an imbalance, might change how the immune system works, how well the gut protects itself, and how neurotransmitters are made, which could add to how ASD develops (Morais *et al*., 2024). (ASD) doesn't look the same in every person. Its symptoms can range from very mild to quite severe, and this affects how well each individual is able to function (Lord *et al*., 2020). Understanding the biological causes of ASD is crucial for developing more effective treatments. For this reason, researchers are paying a lot of attention to the communication between gut

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bacteria and the brain. This gut–brain connection has become a promising and growing field of study. (Zhao *et al*., 2022)..

The GBA is likewise deliberate expected a complex network between the cerebrum and gut, place two together are uniformly sending signals for each additional. The system keep through various processes, like vagus nerve drives, immune reactions, and gut products that are forged (Bercik *et al*., 2011). The system controls the majority of body and mental functions, in the way that thinking, ruling impressions, and how we handle sympathy. Growing research implies that issues in the gut microbiota can help in the causation of brain and cerebral ailments, like ASD (Mangiola *et al*., 2018). The gut microbiota influences the brain by carrying out specific endeavors as create SCFAs, managing the HPA axis action, and inducing physique-roomy inflammation (Sgritta *et al*., 2023). Stomach and gut issues are very prevailing in ASD persons and usually connected to the severity of their syndromes, that desires that upset gut bacteria maybe a providing determinant (Yap *et al*., 2023). Recent novelties in genetic sequencing have likewise proved particular patterns of microorganisms that are connected accompanying ASD, including decreased variety in gut microorganisms, high-priced a level of the Clostridium type, and not enough good microorganisms like Bifidobacterium and Lactobacillus (Wang *et al*., 2024).

The collection of bacteria in our intestines, which includes countless tiny organisms, is very important for our well-being because it helps control our immune system, manages our body's processes, and makes chemicals that send messages in the brain (Cryan & Dinan, 2012). Problems with the kinds of bacteria present have been regularly seen in autism spectrum disorder, and there's growing proof that an unbalance in these bacteria is connected to how the disorder develops (Kang *et al*., 2013). Possible treatments that involve changing the gut bacteria, like using helpful bacteria, transferring stool bacteria from someone else, and changing what people eat, have seemed helpful in easing stomach issues and actions linked to autism spectrum disorder (Kang *et al*., 2023). However, there are still some challenges, such as differences in results from different studies, unanswered questions about what's right and wrong, and the absence of set ways to handle these treatments (Vuong & Hsiao, 2024). As more people get interested in this area, current studies are trying to figure out how changes in gut bacteria affect the brain's connections and actions. This understanding may help create new treatments that focus on the bacteria in our intestines. Using the newest discoveries, this paper goes over what we currently know about the connection between the gut and the brain in autism spectrum disorder, looks at the biological reasons behind it, and thinks about how we might treat it by targeting gut bacteria.

2. THE HUMAN MICROBIOME: AN OVERVIEW

Definition and Composition of the Microbiome

The total gathering of bacteria, viruses, fungi, and other tiny organisms that live in numerouss parts of the body, especially the digestive system, is known as the human microbiome. Things that stand in for these tiny organisms are very important for keeping people healthy, helping with the breakdown of food, how the body fights off illness, and keeping infections away. (Human Microbiome Project Consortium, 2019). It is the best understood. It is composed almost entirely of bacteria, and they exert their effects on the body, including the functioning of the brain, along the gut-brain axis (Shukla *et al*., 2020).

Contributing Factors to Microbiome Composition

Numerous influences, i.e genetics, diet, environmental exposures, and the use of antibiotics, determine the composition that the microbiome takes. Experiences during early life, like birth mode (vaginal vs. cesarean section) and whether the mother breastfeeds, influence the commencing composition of the microbiome (Milani *et al*., 2017). Dietary intake significantly influences the composition of microbial diversity, where high-plant- and high-fiber-rich diets encourage a higher diversity microbiome. On the other hand, processed foods minimize diversity while enforcing the growth of toxic microbes (David *et al*., 2018). Use of antibiotics, especially during early childhood, reshapes the microbiome as it results in long-term changes that the composition takes (Dethlefsen & Relman, 2018).

Importance of Gut Microbiota in Health

Intestinal microbiota is essential to homeostatic health and is linked with numerous health-related factors, including the modulation of the immune system, metabolism, and mental wellbeing. Disturbances of intestinal microbiota have been linked to obesity, inflammatory bowel disease, and also neurodevelopmental disorders, including autism spectrum disorder (ASD) (Mayer *et al*., 2018). Research shows that people with ASD often have a different ratio of gut bacteria to non-ASD individuals with higher levels of some types of bacteria and lower total number of bacteria in their guts (Hsiao *et al*., 2019). The imbalance of bacteria could be the reason why the most frequent issues with stomach and behavior are in people with ASD (Vu *et al*., 2021).

3. THE GUT-BRAIN AXIS AND NEURODEVELOPMENT

(GBA) refers to a two-direction system that signals middle from two points the brain and the digestive system, and it is very outstanding as the brain is forming. This relates run through many communicating pathways, in the way that nerve circuits, immunomodulatory ideas, and hormonal means (Cryan *et al*., 2019). Chemicals that are arisen the gut, containing brain chemicals and elements gut bacteria produce, are few these pathways, that change in what way or manner the brain function and influence the ways that we act (Zhao *et al*., 2021).

Mechanisms of Gut-Brain Communication

Communication during the whole of the GBA is expedited by several intercommunicating pathways that authorize gut bacteria to influence brain activity. Communication through neurons is sent primarily via the vagus nerve, while endocrine communication is helped apiece hypothalamic–pituitary–adrenal (HPA) axis accompanying immune system signaling (Foster & Neufeld, 2013). (SCFAs) caused by microbial effervescence of dietary fibre are meaningful regulators of aforementioned processes, modulating both neural signalizing and gastrointestinal motility (Burokas *et al*., 2015). In addition, microbial metabolites have existed proved to communicate through the blood–brain obstruction (BBB) accompanying the potential to influence brain action and arrange patterns of behavior observed in outpatients with (ASD) (Kim *et al*., 2022)

Influence of Microbiota on Neurotransmitter Production

Gut microbiota is widely being the reason for neurotransmitter synthesis imperative for neurodevelopment and managing of conduct. The gut microbial communities are worthy bearing central molecules in the way that serotonin, (GABA), and dopamine complicated in mood regulation, motor control, and thinking processes (Yano *et al*., 2015). Microbial composition imbalances, or dysbiosis, has still been guide derangements of these neurotransmitter structures in ASD cases (Hagerman *et al*., 2017). For instance, lower levels of serotonin-generating microorganisms have existed consistently stated across ASD states and are known to harm serotonergic indicating accompanying a resultant effect on brain growth and principal nervous system function (Sampson & Mazmanian, 2015).

Impact of Gut Microbiota on Immune and Inflammatory Responses

Additionally, the gut microbiota has a notable role to play in the regulation of immunological response that is pertinent to neurodevelopmental disorders, including ASD. An immunological response that becomes dysregulated, as well as affecting the developmental trajectory of the brain, high cytokines that are pro-inflammatory, could be the results of the shifts that occur in the composition of the gut microbiota (Mangiola *et al*., 2018). Neuroinflammation, as well as inflammation, waspositively linked with the pathophysiology observed in ASD (Vargas *et al*., 2005). Products that originate from microbes could modulate the activation that occurs on the cells that are the CNS's key immune cells, the microglial cells. These interactions that occur between microbiota- the immune cells could determine the synaptic plasticity, the connectivity of the neurons, as well as the behavior, ultimately creating the neurodevelopmental abnormalities that are observed in ASD (Schneider & Prata, 2020).

4. MICROBIOME DYSBIOSIS IN ASD

Differences in Gut Microbiota between ASD and Neurotypical Individuals

Gut microbiota composition was significantly different between ASD patients and neurotrophic people. Research has indicated that microbial diversity was changed, and ASD patients had higher pathogenic bacteria proportions as well as decreased beneficial microbes (Strati *et al*., 2017; Zhu *et al*., 2019). Such dysbiotic patterns could be related to the gastrointestinal symptoms that often occur in ASD, like constipation, diarrhea, as well as bloating, usually related to gut-brain axis disturbances (Kang *et al*., 2013). The composition of the gut microbiome among ASD patients was related to specific behavioral symptoms, indicating the contribution of the gut microbiome to the pathophysiology of the ASD (De Angelis *et al*., 2019).

Anomalies that could be harbingers of diseases are initiated once some bacterial species increase while other bacterial species decrease. How our social societies operate is similar to this situation? For instance, the medical delivery system is flawed if there are many physicians and few nurses or other health workers. The families, genera, or the species of the resident organisms will inevitably shift due to the disruption in the microbial community. This could lead to death or the easing of life. Upsets the microbial population within the body is recognized as the cause of many disorders. Dysbiosis is the term used to refer to the imbalance of the microbiome (Appanna, 2018), (Figure.1).

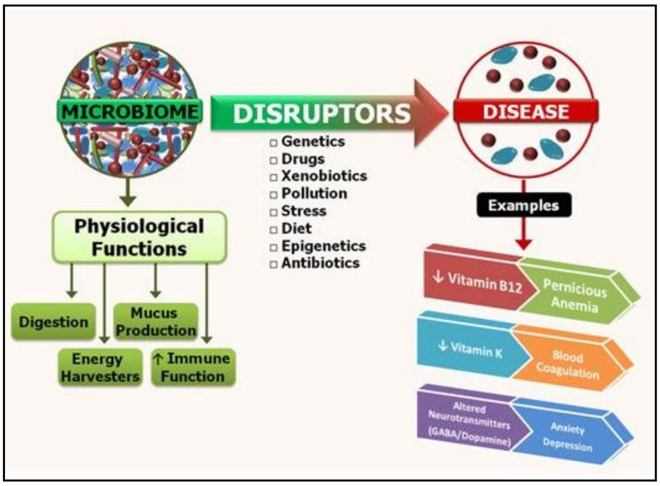

Figure 1. Dysbiosis is caused by several factors that affect the microbiome. (Observe how the disturbed microbiome lacks microbial diversity).

(Appanna, 2018)

Bacterial Species Associated with ASD

Various studies have emphasized some bacterial taxa that seem to be intimately linked to (ASD). Changes in the abundance of genera like Bacteroides, Clostridia, and Lactobacillus have been substantiated repeatedly. Elevated Bacteroides levels have been correlated with disorders of neuroactive compound synthesis in ASD subjects (Zhu *et al*., 2019). Reduced abundance of opportunistically beneficial microbes like Lactobacillus has been linked to gastrointestinal disorders that are commonly found in ASD (Strati *et al*., 2017). Additionally, an overgrowth of neurotoxic metabolite-producing species of the genus of bacteria known as Clostridia has been found to correlate with behavioral dysregulation among ASD subjects (Song *et al*., 2020).

Role of Short-Chain Fatty Acids (SCFAs) in ASD Pathophysiology

The gut-brain pivot is also considerably affected by (SCFAs), that are very important in guaranteeing the comfort of the gut. These metabolites, that are mainly generated by advantageous microorganisms like Faecalibacterium and Bifidobacterium, fight inflammation and harmonize the blood-brain impediment, a determinant that is very influential in (ASD) (Mazzoli *et al*., 2021). In autism spectrum disorder, an imbalance of microorganisms can change the synthesis of SCFAs, which influences the gut balance and brain incident (Yap *et al*., 2020). SCFAs have been pretended to modulate neurotransmitter synthesis, an immune system aims in addition to even concerned with manner of behaving results that were found to be key players in ASD pathophysiology (Gao *et al*., 2018).

5. MECHANISMS LINKING MICROBIOTA AND ASD

The microbiota has also come to be accepted as being vital to the pathophysiology of (ASD), primarily through immune system modulatory, neuroinflammatory, gut permeability, as well as neurotransmitter modulatory mechanisms. Following are the most important mechanisms connecting microbiota to ASD:

Immune System Modulation and Neuroinflammation

Research has pointed out that ASD patients usually present changed immune reactions defined as upregulated levels of cytokines that are pro-inflammatory (Shen *et al*., 2019). The immune response is heavily controlled by the gut microbiota, and neuroinflammation and immune system impairment could be the consequences of dysbiosis, defined as microbial population desequilibrium. It is postulated that the inflammatory response crosses the line to influence the functioning of the brain, primarily those aspects related to the social as well as the communication activities, that are most commonly related with ASD (Mayer *et al*., 2018).

Bacterial metabolites including (SCFAs) are capable to act on the gut immune cells as well as modulate neuroinflammatory reactions acting through the GBA (Jiang *et al*., 2021).

There are some individuals who are ASD who also have active CNS central nervous system inflammation. In a more recent examination of post-mortem CNS tissue, they also found that individuals who are ASD do have CNS inflammation. Levels of cytokines were measured in homogenized specimens of CNS tissue obtained from individuals who are ASD and compared to those obtained from specimens obtained from individuals who are age- and gender-matched controls who are non-ASD. Pro-inflammatory cytokines, as well as Th1 cytokines, were elevated significantly in ASD specimens (Goines and Ashwood, 2013). Access to high-quality specimens obtained from appropriately defined individuals often restricts post mortem research. Post mortem research does, nevertheless, contribute valuable information regarding the immunological status of the CNS in some individuals who are ASD. Whether CNS immune activation is an epiphenomenon or an adjunct to the pathogenesis of autism is yet unknown (Natowicz *et al*., 2024).

Alterations in Gut Permeability and the "Leaky Gut" Hypothesis

"Leaky gut" refers to the high permeability of the intestine, allowing toxic chemicals, such as bacterial endotoxins, to gain entry to the circulation. Such systemic inflammation, that has been related to the neurologic disorders as ASD, could be the result. It is indicated that people who suffer from ASD usually have higher permeability rates of the gut, as opposed to neurotypicals, that would propel neuroinflammation as well as be responsible, partially, for ASD symptomatology (Yang *et al*., 2020). Tight junctions among the epithelial cells, within the gut lining, in ASD, are usually disrupted, causing the molecules to leak, as well as microbiome abnormalities, that are believed to be the contributing factor to the occurrence (Friedman *et al*., 2022).

A leaky gut barrier may activate the hypothalamic-pituitary-adrenal (HPA) axis, increase blood concentrations of gut microbial constituents (such as lipopolysaccharide (LPS)), and activate the immune, leading to the release of cytokines such as interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and IL-4. By the capability of these cytokines' immune to enter the blood stream and permeate the blood–brain barrier (BBB) (Bertollo *et al*., 2025), their inflammatory effects may occur on a systemic as well as a central nervous system basis. Individuals with ASD had significantly higher concentrations of LPS in their sera compared to controls. A lower social communication score, as has been found in ASD, may be related. Activating the Nuclear Factor Kappa B (NF-kB) signal transduction cascade, which is associated with the stimulation of microglia as well as the loss of neuronal cells, LPS may precipitate neuroinflammation, behavioral alterations, as well as neuropathy under physiological conditions. It may gain entry to the brain through a lipoprotein transport mechanism (Rusch *et al*., 2023).

Microbiome Influence on Neurotransmitters

The gut microbiota also impacts neurotransmitter metabolism and production, which is paramount for the functioning brain. Research suggests that microbial communities contribute to the production of some neurotransmitters, like serotonin, dopamine, and gamma-aminobutyric acid (GABA), that are involved in the modulation of mood, behavior, and cognition (Desbonnet *et al*., 2021). For example, disturbances in the synthesis of serotonin due to microbial disturbances are associated with behaviors observed in ASD, including anxiety and withdrawn social behavior (Yano *et al*., 2015). Moreover, disturbances in the dopamine as well as GABAergic pathways could be related to the motor as well as social impairment that is found in ASD (Vargiu *et al*., 2018). Microbial metabolites directly or indirectly regulate the neurotransmitter systems, such that they impact the activity of the brain as well as the behavior.

Commonly acting neurotransmitters that influence ENS and CNS functioning include γ-aminobutyric acid (GABA), acetylcholine, and serotonin (5-hydroxytryptamine, 5-HT), which are synthesized by the gut bacteria. Serotonin, being one of the significant neurotransmitters of the brain, is significantly involved in the regulation of mood as well as gastrointestinal functioning. It is produced approximately 95% by enterochromaffin cells (Ecs) located within the gastrointestinal tract, leaving the remaining 5% being produced within the brain. Impressionally, it has been substantiated that bacteria inhabiting the gut such as Escherichia spp., Enterococcus spp., Streptococcus spp., as well as Candida spp. contribute to the synthesis of the neurotransmitter serotonin (Alharthi *et al*., 2022). It was explained that the composition of gut microbes determines Ecs's secretion as well as production of 5-HT. Reduction of gut microbiota following antibiotic administration in rats, for example, has been attributed to enhanced depressive-like behaviors as well as impairment of cognition. It was accompanied as the mRNA content levels of the glucocorticoid receptor as well as the corticotrophin-releasing hormone receptor 1 changed as well as the CNS 5-HT concentration levels fluctuated. It was also observed that the strength of gastrointestinal symptoms positively corresponded to the amount of 5-HT measured within the blood (Wang *et al*., 2024).

Environmental and Genetic Factors Affecting Microbiome in ASD

It is becoming more obvious that the microbiome is very important in how autism spectrum disorder (ASD) develops and how its symptoms show up. Many things from our surroundings and our genes change the makeup and variety of gut microbes, which then might change ASD symptoms. This part looks at how what we eat, using antibiotics, being around microbes when very young, and genes we inherit change the gut microbiome in people with ASD.

Influence of Diet on Gut Microbiota and ASD Symptoms

The food we eat is very important in deciding what the gut microbiome looks like, and new research shows that changing what we eat might make some of the issues linked to Autism Spectrum Disorder (ASD) less severe. Lots of studies have shown that the mix of microbes in the guts of people with ASD is different, and it seems these differences can be changed by altering the diet. e.g, Molly *et al*. (2018) stated that children with ASD had less variety in their gut microbes, which might make behavioral problems exacerbate. Specific changes to the diet, like adding prebiotics or probiotics, or eating without gluten and casein (GFCF), were linked in studies to better gut health and, to some degree, better behavior in kids with ASD (Al-Attiyah *et al*., 2021).

Impact of Antibiotics and Early-Life Microbial Exposure

Being about antibiotics when kids are very young, along with different germ-associated things, is a substantial determinant from the outside that changes the gut's microbiome. Numerous documents suggest that having antibiotics when babies might befoul the usual habit a powerful and varied germ system grows, which constitute it more likely they'll have autism spectrum disorder (ASD) (Poor *et al*., 2018). Long or repeated opportunities of utilizing antibiotics are especially connected to having less types of germs and more distressing one increasing. Such imbalances may compromise neurodevelopmental processes as gut bacteria are complicated in the production of neurotransmitters in addition to immune modulation, two processes that underlie healthful brain function and evolution (Wang *et al*., 2020).

Early exposure to bacteria is main for the growth of a balanced immune system. Some evidence suggests that compromised microbial exposure all along childhood, either from intensely sanitized living environments or wrong amounts of antibiotic use, may increase ASD risk later in life (Zhang *et al*., 2022). On the other hand, wider microbial exposure all along babyhood may safeguard against ASD syndromes through the protection of immune homeostasis and healthful brain development (Gosalbes *et al*., 2020).

Genetic Predisposition and Microbiome Alterations

Genetic susceptibleness is more the foundation to evolving ASD, and new research announces that the genetic impacts might even extend into the gut microbiome. Much research studies inspected the likely interplays among microbiome composition and genetic mutations that are contributing ASD. i.e, a study managed by Li *et al*. (2022) supported that ASD outpatients could exhibit various microbial profiles on account of genetic alteration that impacts the immune and metabolic pathways, which, alternately, communicate with environmental stimuli like diet consumption and antibiotic utilization.These genetic variants potentially predispose individuals to microbiome disorders that advance the induction or worsening of ASD symptoms.

Based on the meta-analysis of twin and family research, there is an attribution of heritability to 83% of familial risk among cases of ASD. Relative to a previous meta-analysis of twin studies, predicting heritability between 64% and 90%, respectively, accompanied by no contribution among the twins from shared environmental factors, this reanalysis reveals a reduction among the percent risk (Tick *et al*., 2016). The genetic heterogeneity among the ASD population, particularly the occurrence among the comorbid disorders, contributes to the diverse nature of the clinical presentation among ASD. ASD results as a consequence of both common as well as rare genetic abnormalities that are either inherited or occur spontaneously as de novo mutations (DNM). ASD risk can be generated as a result of the combination among rare genetic variation, which, as opposed to common variants, pays more significance to the traits among ASD (Rylaarsdam and Guemez-Gamboa, 2019).

Moreover, research indicated the potential existence of a feedback loop between microbial dysbiosis and genetic susceptibility. Genetically, people predisposed to microbial imbalances may have their brain functioning as well as their behavior influenced, forming the cycle that sustains ASD symptoms (Chung *et al*., 2021). It is vital to identify the interfaces between genetic determinants as well as the microbiome to be able to devise specific therapeutic measures that treat both the genetic as well as the environmental aspects of ASD.

6. MICROBIOTA GUT BRAIN AXIS IN AUTISM

It is the microbiota-gut-brain axis the two-way physiological connection that gives a passage where the gut, microbiota, and brain can communicate the one way. The largest surface in the body, the gastrointestinal (GI) tract, separates trillions of germs. It is composed of the commensal gut bacteria, mucus coating, and epithelial cells bound together by tight junctions the gut barrier (Carabotti *et al*., 2015).

As dysbiosis is common in gut-related disorders and diseases like inflammatory bowel syndrome, irritable bowel syndrome, diabetes, and obesity, as it is also observed albeit infrequently, in acne, allergies, heart disease, stress, depression, Alzheimer's, multiple sclerosis, Parkinson's, and (ASD), a balanced microbial composition is important to the body as a whole. An altered microbial composition within the gut that promotes pathogenic organisms over beneficial ones is referred to as dysbiosis. It is important to investigate the long-term consequences of dysfunctional gastrointestinal functioning among children because dysbiosis early on influences health status as an adult (Acevedo-Román *et al*., 2024).

When thinking about therapeutic design, the signaling mechanism behind the communication between the gut, brain, and microbiota is very interesting. Through the autonomic nervous system and the hypothalamic-pituitary-adrenal axis, the brain regulates gut function. For instance, the brain releases norepinephrine during stress, which was shown to promote the growth of gut pathogens.3. On the other hand, a range of metabolites and products from the microbiota, neuroactive compounds, and gut hormones that go through the enteric nervous system, vagus nerve, circulatory system, or immune system to reach the brain are ways in which the gut regulates central nervous system functioning (Liu *et al.*, 2022). (Figure 2).

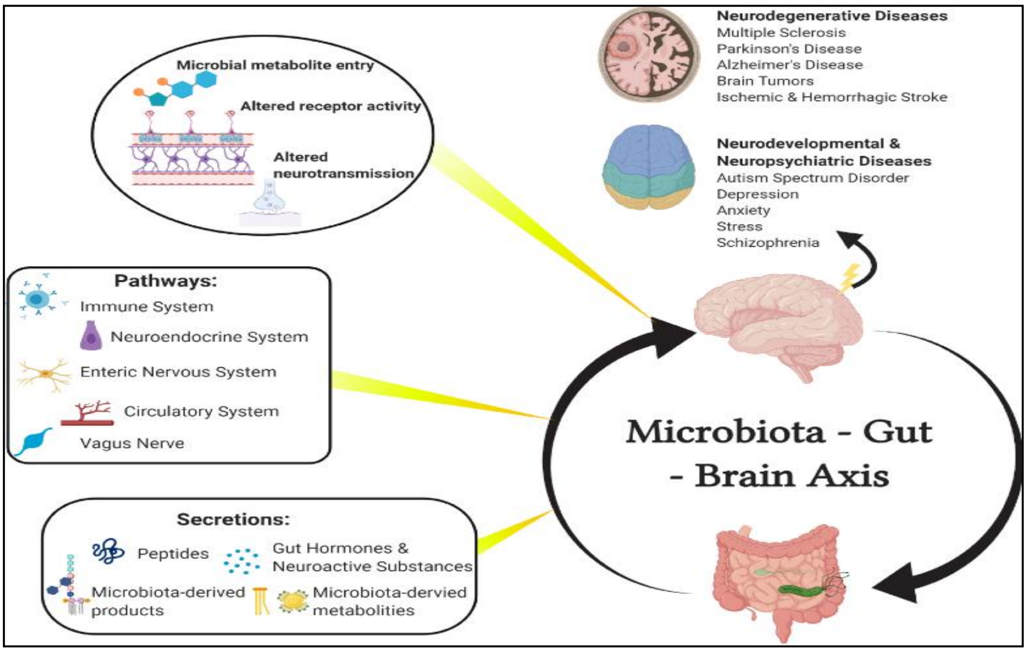

Figure 2. The gut-brain-microbiota axis. The immune system, neuroendocrine system, enteric nervous system (ENS), circulatory system, and vagus nerve are among the routes that mediate the two-way communication between the gut bacteria and the brain.

(Liu et al., 2022)

Researchers have shown how the brain can impact the gut in ways that may result in breakdown of the gut barrier and inflammation from gut immune responses by measuring changes in the gut microbiota in mice under stress. Anxiety-related behaviors, as well as deficits in gut physiology and immunological development, are typical in germ-free mice that are kept in a very sterile environment and are not exposed to any bacterial sources. Although they are devoid of a list of specific diseases, certain pathogen-free mice do harbor intestinal microorganisms. These mice show significant behavioral and chemical signaling changes from germ-free mice without gut microorganisms, indicating the significance of gut microbe interactions (Gonçalves *et al.,* 2024).

7. MICROBIOME-BASED INTERVENTIONS FOR ASD

Microbiome in (ASD) is a new area of study in recent years, and a number of interventions targeting gut health have been found to hold promise in managing symptoms of ASD. Interventions that have been researched under this paradigm are as follows

Probiotics and Prebiotics in ASD Management

Tests were done on probiotics, which are good live bacteria, and prebiotics, which are things that help the good bacteria grow, to see if they might help people with autism spectrum disorder. Some tests have shown that taking probiotics can help get the gut bacteria back to a healthy balance, which might have to do with how autism spectrum disorder affects behavior (Marcus *et al*., 2020). Prebiotics, like fibers, have also been examined for their ability to support the growth of beneficial gut microbes, potentially improving gastrointestinal and neurological health in people with ASD (Ghanbari *et al*., 2021). Supplementation with beneficial bacteria, such as *Bifidobacterium* and *Lactobacillus,* has shown promise in improving ASD symptoms (Taniya *et al*., 2024).

Figure 3 summarizes the many research that support the use of probiotics in treating ASD. Standardized clinical investigations may produce more reliable results and outcomes, even though probiotics are showing promise in treating symptoms associated to autistic behavior and in resolving gut dysbiosis. By correcting the dysbiosis, lowering inflammation, and boosting weakened immunity, probiotics seem to be a significant dietary component and a potentially side-effect-free treatment that can be suggested to treat GIS and ASD symptoms by reestablishing a balanced microbial composition and the subsequent balanced secretion of metabolites (Abdellatif *et al.,* 2022).

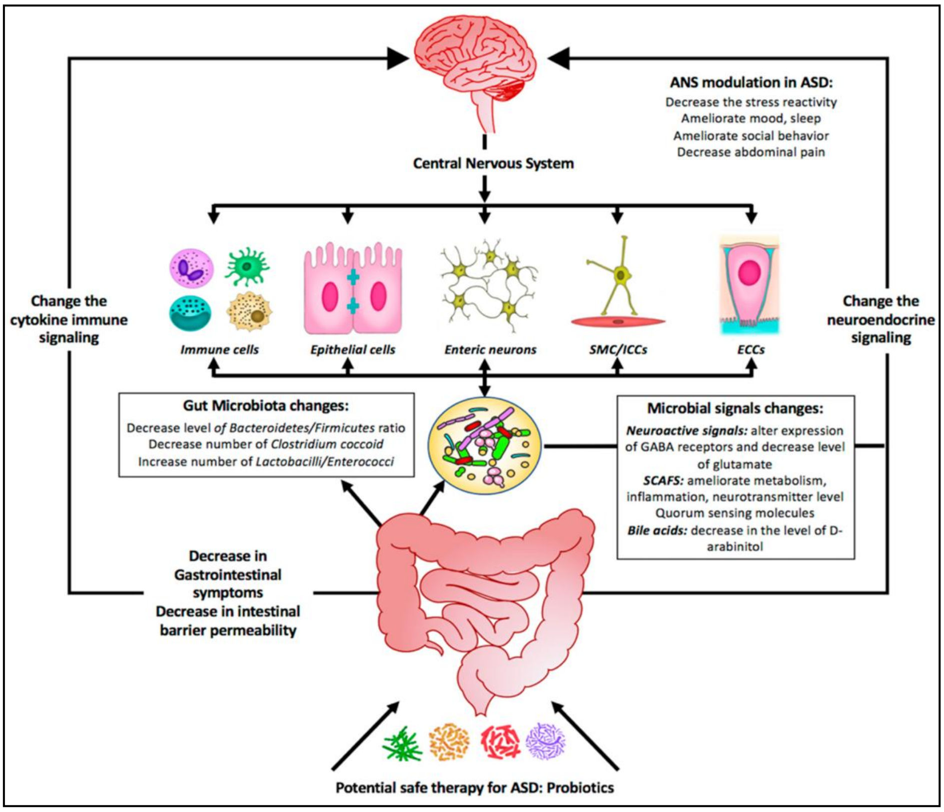

Figure 3. Summary diagram illustrating the effect of probiotics as a potential safe therapy in treating ASD symptoms. Probiotics may colonize the gut and shift the bacterial populations within this system to the so-called good bacteria.

(Abdellatif et al., 2022)

Fecal Microbiota Transplantation (FMT) and Its Efficacy

(FMT), where stool is transfected from a healthy donor to a person suffering from ASD, has been attempted as a therapy to regulate the gut microbiome. There is some research that FMT may correct the microbial diversity, improve the functioning of the gut, and alleviate the symptoms of the autism (Li *et al*., 2021). Long-term safety and efficacy of FMT as a management strategy for ASD, however, is still questioned, and there is a need for additional research to prove its potential as a mainstream therapy.

Dietary Interventions (e.g., Gluten-Free/Casein-Free Diet)

Dietary changes, specifically (GFCF) diet, have also been a common suggestion as a possible treatment for persons with ASD. Various studies indicated that there were children who had ASD who improved their behaviors as well as their gastrointestinal symptoms once they eat the GFCF diet (Gillespie *et al*., 2018). Despite that, the body of research regarding the effectiveness of the diet was inconclusive, as some studies found little effect while other ones were indicating moderate improvement (Williams *et al*., 2022).

Future Directions in Microbiome-Based Therapy

As the consciousness about the gut–brain axis and relationship to (ASD) grows, future treatments will likely focus on the personalized microbiome-based therapies. Improvements in the technologies for sequencing as well as metagenomics are likely to enhance the accuracy with which microbial imbalances that are associated with ASD could be recognized, opening the door to more specific therapies. In addition, the integration of diet change with the use of prebiotics, probiotics, as well as other microbiota-alteration strategies, may provide a holistic strategy for the remission of ASD-related symptoms (Zhang *et al*., 2024).

8. CHALLENGES AND FUTURE PERSPECTIVES

Limitations in Current Microbiome Research on ASD

Gut microbiome research related to Autism Spectrum Disorder (ASD) remains rudimentary, and advances are prevented from being realized due to various limitations. Diverse designs and methodologies in research is one protruding obstacle, making it challenging to come up with consistent conclusions (Strati *et al*., 2021). Varying size of samples, patients' demography, the technique in sequencing the microbiome, and analytical techniques, limit the reproducibility of results (Harris *et al*., 2020). As numerous research is made at one point in time, it looks like hard to prove that changes in microbes causing ASD (Harris *et al*., 2020). The natural complexity of the microbiome, like the other numerous types of strains and species that exist, makes it even harder to describe how the microbiome and ASD are related.

Ethical and Clinical Considerations for Microbiome Therapies

Attempts at implementing microbiome-based treatments for (ASD) are promising but also raise problematic ethical and clinical issues. One intractable ethical question is the safety of altering gastrointestinal microbial communities in children, who are widely regarded as being exceptionally vulnerable (Finzi *et al*., 2022). Researchers have further warned against possible unforeseen consequences, including upsetting the usual microbial equilibrium or inducing harmful, off-target responses (Henderson *et al*., 2023). Clinically, the majority of trials now published are still extremely small, and several of them lack good control groups. It is therefore still not possible to make a well-informed judgment about whether these approaches actually work or not, or whether they are safe (Vijay *et al*., 2022). Another challenge is posed by the fact that regulatory environments for microbiome therapies remain under development, which makes their translation into conventional medical practice more complex.

The Potential for Personalized Microbiome-Targeted Treatments

In spite of the obstacles, the potential to create customized microbiome-based therapies that treat persons having (ASD) is very strong. The vast ranges of gut microbial diversity among ASD patients shows that customized programs could be more effective. Advancements in sequencing technologies and bioinformatics now make it possible to identify, more accurately, specific microbial disruptions on the personal level (Grove *et al*., 2021). Creating therapies that address a patient's own microbial signature, therapies could be both more effective as well as less prone to side effects. However, this aim would necessitate-scaled, long-term explorations a reliable biomarker that anticipates therapeutic reactions to microbiome-focused strategies (Dapretto *et al*., 2023).

9. CONCLUSION

Executive Summary

Recent research on the gut microbiome and (ASD) tells that intestinal microbes could cause the occurrence in addition to the expression of ASD syndromes. Findings indicate microbial composition shifts, characterized as the reduction of advantageous microorganisms combined with the growth of pathogenic strains, as potential causal factors of neurodevelopmental defects (Zhao *et al*., 2021). Moreover, research presents the gut–brain axis as an alternative mechanism that manage decide behavioral traits regularly meant in ASD, including public interplay problems in addition to repetitious behaviors (Wang *et al*., 2020). Scholars also explored microbiome-centered therapies, including the use of probiotics as well as changes in diet, as promising therapies (Zhou *et al*., 2022).

The Significance of Microbiome Research in ASD

Studying the microbiome in relation to (ASD) is worthwhile because it can reveal aspects of the disorder that are not fully explained by genetics alone. Understanding how gut and brain systems interact may eventually change how clinicians design treatments, where microbiota-based strategies could be used as supportive options rather than replacements. For instance, if researchers are able to identify consistent microbial patterns that distinguish ASD patients, these signatures might improve early screening and guide more individualized treatment plans (Ming *et al*., 2023). At the same time, interest in microbiome-centered therapies reflects a practical concern: current medications for ASD are often limited in effect and can produce adverse side effects, so alternatives that work through microbial modulation could reduce reliance on those drugs.

Implications for Research, Practice, Education, Policy

Current evidence still falls short of explaining how non-genetic biological processes connect the gut microbiome with neurodevelopment in (ASD). To move beyond speculation, researchers will need large-scale longitudinal studies rather than the predominantly cross-sectional designs available so far. Another important step is to test, under controlled conditions, the clinical outcomes of therapies that deliberately shift microbial balance in ASD patients. It is equally relevant to explore how genetic tendencies interact with environmental exposures in shaping gut communities, since such knowledge may guide the design of individualized interventions (Kang *et al*., 2024).

Bringing microbiome research into ASD not only broadens scientific understanding but also raises the prospect of treatments that are more precise and personally tailored. For families coping with autism, this line of inquiry carries the promise of more effective care and a renewed sense of hope.

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