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Re-examining the Controversial Case of 'Autistic Enterocolitis': The Role of Gut-Brain Axis in Autism Spectrum Disorder

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Abstract

This paper re-examines autistic enterocolitis (AuEC) which the authors believe is crucial due to its implications for understanding and managing autism spectrum disorder (ASD) and associated gastrointestinal (GI) symptoms. Despite its controversial origin, with the discredited 1998 study of Wakefield et al., many individuals with ASD experience significant GI issues - abdominal pain, diarrhea, and constipation - that affect their quality of life. Emerging research on the Gut-Brain Axis suggests potential biological links between ASD and GI dysfunction, including differences in gut microbiota, immune responses, and the heritable traits of gut microbiome. The aim of this paper is to revisit the concept of AuEC with evidence-based studies to make constructive sense of the controversy, leading to more holistic treatment approaches that address both behavioral and GI symptoms. By objectively investigating AuEC, authors hope to advance knowledge and improve care for those with ASD.

Keywords: *Autistic Enterocolitis, Gastrointestinal (GI), Gut-Brain Axis (G-BA), Microbiome, Wakefield*

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Introduction

Autistic Enterocolitis (AuEC) has been a controversial term - not recognized in the mainstream gastroenterology and psychiatry - since it was first proposed in 1998 to describe gastrointestinal (GI) inflammation in individuals with autism spectrum disorder (ASD) (see Wakefield et al., 1998; also see BMJ Editorial Board, 2010). The authors of this paper are quite aware that the term is misleading and it perpetuates discredited theories linking ASD and GI disease to vaccine injury, especially the Measles-Mumps-Rubella (MMR) vaccine. This contentious concept emerged from observations that many children with ASD also experience GI issues: e.g., diarrhea, constipation, and abdominal pain. The term AuEC gained a significant attention towards the end of 1990s and at the beginning of the new millennium, especially, in the early 2000s. However, AuEC has since become a taboo among academics, practitioners and clinical researchers studying ASD and a subject of intense debate within the psycho-medical community.

The question of why re-examining the controversial case now? The authors felt that it is timely to do so in view of the recent 3-day Second Annual Autism Health Summit (known for its polarizing anti-vaccine autism campaign) held in San Diego, California, where "presentations about treatments that promise miracles to help heal the condition - water filters and electromagnetic gadgets, supplements, stem cell treatments only available in Europe, and fecal transplants here in the U.S." (Zadrozny, 2025, para. 1), strongly supported by Robert F. Kennedy Jr. (the current Health and Human Services Secretary in the Trump administration), who is also known to be an anti-vaccine lawyer and activist. It is worthwhile to re-examine the controversial condition of autistic enterocolitis for three reasons: firstly, the authors hope to disentangle valid GI concerns from discredited vaccine-autism claims. Secondly, they want to highlight the emphasis on client well-being, evidence-based practice, and ethics in ASD research. Lastly, the authors argue the need for better treatment for GI issues in autistic individuals that have always been overlooked or misunderstood.

It is well-documented that children with ASD are more likely to have GI symptoms (e.g., constipation, diarrhea, and abdominal pain) compared to their neurotypical peers (Chogle, Wong, & Megerian, 2024). These symptoms are now being studied more rigorously, but not as a cause of autism, rather as comorbid conditions that may exacerbate behaviors or discomfort (Hung & Margolis, 2024; Kennedy et al., 2024; Li et al., 2024). Studies (e.g., Al-Beltagi et al., 2023; Buie et al., 2010; Leader et al., 2022) indicate that these symptoms can significantly impact the quality of life and may exacerbate behavioral issues. However, the exact nature of the GI pathology in ASD remains very much unclear and heterogeneous (also see Prabhakaran et al., 2025, for detail).

Research (e.g., Bjørklund et al., 2020; Coury et al., 2012; Krigsman & Walker, 2021) exploring the pathophysiology of GI symptoms in this so-called condition of AuEC has examined various factors, including gut microbiota, immune responses, gut microbiome heritability, and dietary influences. Several studies (e.g., Adams et al., 2011; Brüssow, 2020; de Theije et al., 2014) suggest dysbiosis, which is an imbalance in the gut microbiota, and an increased intestinal permeability, often referred to as the 'Leaky Gut Syndrome' (LGS; Camilleri & Vella, 2022), a controversial condition not currently recognized in the medical field, in children with ASD.

Clinical therapists treating children with ASD and GI symptoms often adopt a multidisciplinary approach, addressing dietary needs, potential allergies, and behavioral therapies. While some interventions, such as dietary changes and probiotics, show promise, more rigorous and controlled studies are needed to establish effective treatments (Buie et al., 2010; Newnham et al., 2009).

The origin of the concept of AuEC can be traced to the controversial study done by Wakefield et al. (1998) published in *The Lancet*. The authors reported a new syndrome and coined the term 'autistic enterocolitis' and claimed that the condition involved GI abnormalities and developmental regression in children with ASD. This contentious concept emerged from observations that many children with ASD experienced GI-related problems including diarrhea, constipation, and abdominal pain.

The Controversy of Autistic Enterocolitis

The condition of autistic enterocolitis (AuEC for short) was introduced by Wakefield et al. (1998) in their controversial paper *Ileal-Lymphoid-Nodular Hyperplasia, Non-specific Colitis, and Pervasive Developmental Disorder in Children* published in The Lancet. Briefly, the study reported on 12 children with developmental disorders, including ASD, who were said to have a novel form of bowel disease featuring inflammation of the colon and small intestine. It had also made a contentious claim that there was an association between the measles, mumps, and rubella (MMR) vaccine and ASD.

Interestingly, the hypothesis suggested that the MMR vaccine might have caused intestinal inflammation, allowing harmful proteins to enter the bloodstream and affect the brain development, and thus, contributing to the onset of ASD (Wakefield et al., 1998). As a result, this hypothesis gained a significant public attention and led to widespread concern about the safety of the MMR vaccine.

However, following the claims made by Wakefield et al. (1998), several subsequent large-scale epidemiological studies (Chen et al., 2004; DeStefano & Shimabukuro, 2019; Fombonne & Cook, 2003) were undertaken to replicate their findings using their respective research methodologies, but failed to conclude with the same findings, i.e., to confirm a link between the MMR vaccine and ASD (Cosenza & Sanna, 2023; Steinmetz, 2023). Additionally, these studies did not consistently find a unique inflammatory bowel disease specific to children with ASD (DeStefano & Shimabukuro, 2019; Madsen et al., 2002; Taylor et al., 1999). It was later, the research ethical standards came under intense scrutiny.

Investigations revealed serious procedural errors, undisclosed financial conflicts of interest, and ethical violations in the work of Wakefield et al. (1998), which has since been discredited and retracted. It was after 12 years that in 2010, *The Lancet* formally retracted the 1998 "paper that sparked an international crisis of confidence in the safety of the measles, mumps, and rubella (MMR) vaccine when its lead author suggested a link between the vaccine and autism" (BMJ, 2010, para. 1). According to *The Lancet* editors, "Following the judgment of the UK General Medical Council's Fitness to Practise Panel on Jan 28, 2010, it has become clear that several elements of the 1998 paper by Wakefield et al. are incorrect, contrary to the findings of an earlier investigation" (BMJ, 2020, para. 4). The lead author, Dr

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Wakefield, was eventually stripped of his medical license by the UK General Medical Council for his professional misconduct.

The concept of AuEC remains highly controversial even today and the pseudo-condition (as one might want to term it) is not recognized or accepted by the mainstream medical community. Extensive research has shown no causal link between the MMR vaccine and ASD (Bustin, 2013; Steinmetz, 2023). The current scientific consensus is that ASD is far more complex as a neurodevelopmental disorder with a strong genetic basis, too. Environmental factors may also play a role, but vaccines, including the MMR vaccine, are not among them.

Generally, GI issues have been reported more frequently in individuals with ASD compared to the general population. These issues, as mentioned earlier in the introduction, can include constipation, diarrhea, and abdominal pain, and they may exacerbate behavioral symptoms in some individuals. However, the exact relationship between ASD and GI problems remains not fully understood. Several theories (e.g., Liang, Wu, & Jin, 2018; Mayer, Nance, & Chen, 2022; Miller, 2018) have been put forward to explain the GI issues, and they include shared genetic factors (Gong et al., 2023; Lee et al., 2021) affecting both gut and brain (or Gut-Brain Axis; G-BA for short) development, and differences in diet and lifestyle among individuals with ASD.

Despite the discredited origins of AuEC as a syndromic condition, the idea that GI health can impact neurological and behavioral conditions has driven further research. Research studies (e.g., Kim, 2024; Morton et al., 2023; Sherman, Zaghouani, & Niklas, 2015) have been carried out, exploring the Gut-Brain Axis (G-BA), i.e., the complex communication network between the gastrointestinal tract and the central nervous system. This paper aims to re-examine the concept of AuEC to better understand how gut health might influence neurological development and function, including in those with ASD.

In short, despite the term ‘autistic enterocolitis’ (AuEC) originated from a debunked and discredited study (Wakefield et al., 1998; BMJ Editorial Board, 2010), the broader investigation into the connections between GI health and ASD remains important and continues, driven by the recognition that individuals with ASD often experience significant GI symptoms that can impact their quality of life. What is more important is to seek to improve the quality of life for affected individuals through targeted treatments and interventions.

What exactly is Autistic Enterocolitis?

It is important to reiterate (and also to clarify) that autistic enterocolitis (AuEC) is not recognized as a medical condition by mainstream psycho-medical authorities such as the American Academy of Pediatrics, the Centers for Disease Control and Prevention (CDC), or the World Health Organization (WHO). However, for the purpose of our discussion in this paper, we will proceed under the assumption that AuEC is a so-called ‘valid’ condition for re-examination here.

The term autistic enterocolitis (AuEC) consists of two key components: (1) autism (Au) or autism spectrum disorder (ASD), and (2) enterocolitis (EC). The former is a developmental disorder with broad endophenotypes, i.e., familial, heritable, and quantitative traits associated with a complex disease, occupying an intermediate position between genotype and behavior (Persico & Sacco, 2014), is characterized by challenges in social interaction, communication, and restricted or repetitive behaviors. Autism/Au or ASD is considered a neurodevelopmental condition with a range of presentations and severity levels (Joon, Kumar, & Parle, 2021). The latter refers to inflammation of the intestines, specifically involving both the small intestine (enteritis/E) and the colon (colitis/C). The term entercolitis/EC is used to describe various inflammatory conditions affecting the GI tract.

As already explained earlier, the concept of AuEC arose from the hypothesis of Wakefield et al. (1998) and it claimed that certain GI symptoms, such as inflammation and abnormal intestinal permeability (also commonly known as ‘leaky gut’ - a hypothetical and medically unrecognized condition), could be associated with ASD. The authors of the Wakefield et al paper had proposed that these GI issues might contribute to or be a manifestation of ASD. Galiatsatos, Gologan, and Lamoureux (2009) examined the controversial AuEC by reviewing existing literature and evidence, and also discussing the GI symptoms often observed in children with ASD. They critically analyzed these symptoms that constituted the distinct pathological condition of AuEC, and finally drew their own conclusion stating that current evidence failed to support the existence of AuEC as a unique disease. Moreover, subsequent scientific research and extensive investigations have failed to establish a causal link between vaccines, gastrointestinal issues, and ASD. Hence, the original study of Wakefield et al. (1998) was retracted due to serious methodological flaws and ethical concerns, and subsequent large-scale studies have consistently shown no evidence of a connection between vaccines and ASD (also see BMJ Editorial Board, 2010).

In summary, AuEC continues to remain a controversial and discredited term that emerged from a now-debunked hypothesis linking vaccines, GI inflammation, and ASD. It is not recognized as a valid psycho-medical condition, and there is no scientific evidence supporting its existence or its role in the etiology of ASD (Galiatsatos, Gologan, & Lamoureux, 2009; MacDonald & Domizio, 2007).

Gut and Gut Microbiome

Moving forward, the authors of this paper proceed to explore gut and gut microbiome. The word ‘gut’ can be simply referred to the GI tract, which is composed of various hollow organs, aligned linearly, involving mouth, esophagus, stomach, small intestine, large intestine (colon), rectum, and anus. It is where food eaten and liquid drunk are digested and its nutrients are absorbed. It is also where harmful waste materials are removed from the body. Not forgetting that the intestines contain billions of bacteria (referred to as microbiome) that are responsible for many different bodily functions (e.g., digestion, immunity, and general well-being of an individual (Salvadori & Rosso, 2024).

In other words, “The human gut harbors a complex community of microbes that profoundly influence many aspects of growth and development, including development of the nervous system. Advances in high-throughput DNA sequencing methods have led to rapidly expanding knowledge about this gut microbiome” (Mulle, Sharp, & Cubells, 2013, p. 1). In short, the gut is home to a complex community of microorganisms collectively known as the gut microbiome (GMb). As mentioned, this microbiome contains microbes which include bacteria, viruses, fungi, and other

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microbes. These microorganisms play a crucial role in various bodily functions, including digestion, metabolism, immune system regulation, and even influencing mood and mental health.

The GMb plays a crucial role in breaking down food, producing essential vitamins, and protecting against harmful pathogens. An imbalance in the GMb - known as dysbiosis - can result in various health issues, e.g., GI disorders, obesity, diabetes, and even mental health challenges including ASD (Doenyas, 2018). Hence, the relationship between the gut and the microbiome is essential for maintaining one's overall health and well-being, especially more so for those with ASD.

However, the gut does not exist or operate alone. It is also linked to the brain via the tenth cranial nerve known as *vagus nerve*. This nerve connects the brain to various organs, helping it to regulate vital functions like heart rate, digestion, and respiration. Hence, the vagus nerve serves as a main channel for neural communication between the gut and the central nervous system (CNS) of the brain. The Gut-Brain Axis (G-BA) represents a bidirectional communication system that facilitates the transmission of signals between the GI tract and the brain (see Figure 1) (Labrenz et al., 2023). Approximately 80 to 90% of the vagus nerve fibers are afferent in nature, transmitting information from the GI tract to the central nervous system (Ottaviani & Macefield, 2022).

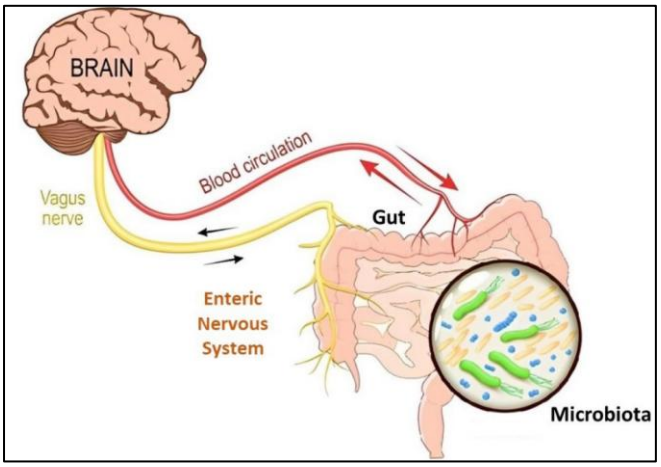

Figure 1. The Gut-Brain Connection (Labrenz et al., 2023)

The Gut Microbiome (GMb) plays an important role in early brain development, and disruptions to it (known as dysbiosis) during critical developmental stages can interfere with the G-BA, which, in turn, affects the brain development and function through neuropathways, such as the neuroendocrine, neuroimmune, and autonomic nervous systems (Li et al., 2023). Such disruptions to brain connectivity and functionality have been associated with mental health and neuropsychiatric disorders (De Sales-Millán et al., 2023; Wong, Montgomery, & Taylor, 2021). This condition may also contribute to the manifestation of what is now called the Leaky Gut Syndrome (LGS) mentioned earlier. Such permeability can give rise to overall inflammation, allowing the entry of bacterial byproducts into the bloodstream. This pathway has been observed to impact neurological functions, as evidenced in numerous individuals with ASD.

Findings from two randomly selected recent studies carried out by Liu et al. (2019) and Wong, Montgomery and Taylor (2021) have indicated that modifications in the G-BA may play a significant role in contributing to GI symptoms as well as behavioral manifestations in children with ASD. These children exhibit unique GMb profiles, characterized by a notable reduction in overall microbial diversity and significant alterations in the levels of specific bacterial genera, in comparison to their neurotypically developed counterparts (see Zuffa et al., 2023) (also refer to Appendix 1 for more detail). Longitudinal studies have identified variations in the composition of the GMb as early as five months of age in infants with an increased risk of developing ASD (Wernroth et al., 2022).

However, in the detailed literature review over past six months, the second author of this paper found that there is still a lack of clear consensus on the specific bacterial taxa or magnitude of changes associated with ASD. Additionally, all the three authors of this paper have concurred with each other that the relationship between these microbial changes and ASD symptoms is still being investigated, and causality has not been definitively established (also see Korteniemi, Karlsson, & Aatsinki, 2023).

Genetics on Gut Microbiome in Autism

Genetics can influence the GMb in individuals with ASD (Goodrich et al., 2016; Liu et al., 2021). Heritability studies (e.g., Grieneisen et al., 2021; Lopera-Maya et al., 2022; Rothschild et al., 2018) have indicated that human genetics could explain from 1.9% to 8.1% of gut microbiome variation.

The genetic makeup of an individual with ASD can affect their immune system, gut barrier function, and metabolism (Cheng, Rho, & Masino, 2017; Liu et al., 2021; Yousefi et al., 2022). These factors can indirectly influence the composition and diversity of the GMb. In addition, the genetic variants related to immune function can impact how the immune system interacts with gut microbes (Hall, Tolonen, & Xavier, 2017). Alterations in immune responses and inflammation can lead to changes in the GMb composition. Moreover, genetic variations in metabolic pathways can affect how nutrients from the diet are processed and utilized by both the individual with ASD and the GMb. These variations can influence which microbes thrive in the gut environment. Besides, genetic factors can also influence dietary preferences and behaviors, and, in turn, affect the types of foods consumed (Smith et al., 2016). Hence, diet plays a crucial role in shaping the GMb, so genetic predispositions towards certain diets can indirectly impact microbial communities. Finally, genetic factors can potentially influence the types of microbes that colonize the gut early in life (Vandenplas et al., 2020). This initial microbial colonization can have long-term effects on the GMb development in an individual with ASD (Sarkar et al., 2021).

While genetics can influence the GMb in those with ASD, there are also environmental factors (e.g., diet, antibiotics, and environmental exposures) that play significant roles in shaping the GMb composition (Dong & Gupta, 2019; Rinninella et al., 2019). The interplay between genetic predispositions and environmental influences is complex and continues to be an active area of research in understanding the G-BA and its implications for ASD (see Wang et al., 2023). How genetics affects the G-BA can be briefly explained as follows: Firstly, there are genetic variants affecting the nervous and immune systems. The synaptic genes (e.g., NLGN3, NRXN1, and SHANK3) not only influence the development of the brain (Zhang et al., 2024), they also affect the enteric nervous system (Wang et al., 2023) that governs gut motility and signaling. The immune-related genes (e.g., HLA and MET) modulate inflammatory responses, and their variants can

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lead to chronic low-grade inflammation, impacting both G-BA in terms of brain development and gut function (Rutsch, Kantsjö, & Ronchi, 2020; Vanuytsel, Bercik, & Boeckxstaens, 2023). Secondly, genetic influence on gut microbiome composition can indirectly shape the GMb, influencing the immune system function, the mucosal barrier integrity and the GI motility (Basson et al., 2016; Sartor, 2010). The differences in the gut microbiome, in turn, produce neuroactive compounds (e.g., GABA, serotonin, and short-chain fatty acids), impacting the brain function, especially in those cortical areas relating to behavior and emotion (Jadhav et al., 2022; Silva, Bernardi, & Frozza, 2020). Thirdly, the serotonin pathway genes, which an estimated 90-95% of the serotonin is produced in the gut (Kim & Camilleri, 2000). For instance, the SLC6A4 (serotonin transporter gene) can affect serotonin reuptake and availability (Ho et al., 2013). Abnormal serotonin signaling has been found to link to both GI symptoms and behavioral traits in ASD (Hsiao, 2014; Israelyan & Margolis, 2019; Wasilewska & Klukowski, 2015). Fourthly, there are also the barrier integrity genes (see Gieryńska et al., 2022, for detail), which affect the intestinal epithelial barrier (e.g., CLDN, which encodes claudins). This can lead to the controversial 'leaky gut syndrome' (LGS, which has been dismissed as a 'fad' diagnosis; see Barrett, 2018) and thus, it increases the systemic exposure to microbial metabolites and inflammatory molecules, which, in turn, may influence brain development and behavior (also see Camilleri & Vella, 2022). There have been claims for the existence of LGS as a distinct medical condition come mostly from nutritionists and practitioners of alternative medicine (Barrett, 2018; Odenwald & Turner, 2013). Lastly, there are also the mitochondrial and metabolic genes (e.g., SLC25A and UCP2 have been found to affect those with Alzheimer's disease; see Crivelli, Gaifullina, & Chatton, 2024) whose mutations can impair energy metabolism, impacting the G-BA (i.e., both gut function and neural activity) and, as a result, these mutations can also contribute to autistic symptoms. According to Palmieri and Persico (2010), "[T]hese biochemical abnormalities are accompanied by highly heterogeneous clinical presentations, which generally (but by no means always) encompass neurological and systemic symptoms relatively unusual in idiopathic autistic disorder" (p. 1130). In summary, the genetic factors can influence the neurodevelopment of the brain directly, the gut structure and its function as well as the composition of the gut microbiome. In terms of the immune responses, these effects together shape the G-BA, possibly contributing to both core traits of ASD and its common comorbidities (e.g., anxiety, GI disturbances, and sensory processing differences).

Figure 2 provides a simple diagramatic summary on the genetic influence on the Gut-Brain Axis (G-BA) in ASD through the interconnected pathways among the four key components: (i) Genetics; (ii) Brain; (iii) Gut; and (iii) Gut Microbiota (GMb). The genetic variants, i.e., those which affect the nervous and immune systems, and also the genes that are involved in the serotonin pathways, barrier integrity as well as the mitochondrial function, can impact on G-BA. These genetic factors can alter brain neurodevelopment and behavior as well as gut function and its structure. As a result of the changes in the gut, the composition and activity of the GMb that produces metabolites can further impact the brain function, completing a bidirectional feedback loop critical to ASD-related traits.

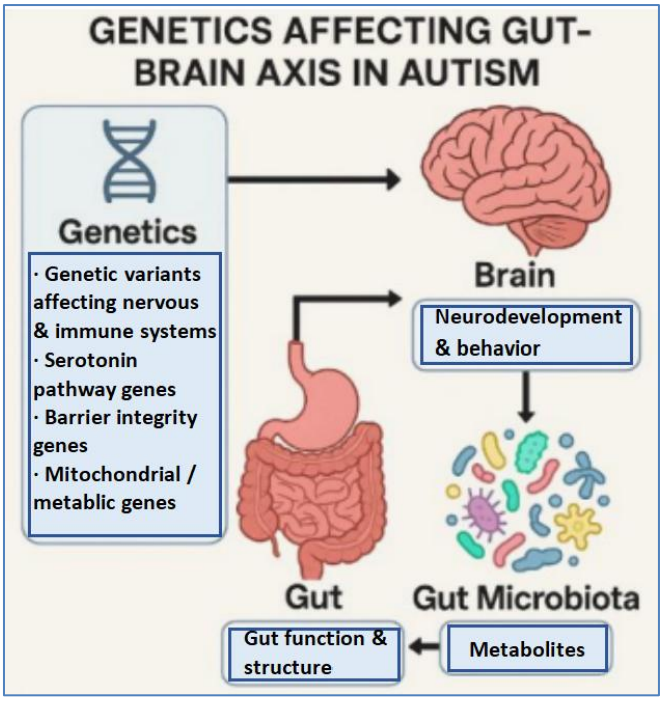

Figure 2. Genetic Influences on Gut-Brain Axis in ASD

Concluding Summary

The re-examination of the AuEC in this paper is necessary due to its potential implications for understanding and managing ASD and its associated GI symptoms, despite its controversial origin. The authors of this paper have identified and summarized five key factors associated with the concept as follows:

- The first factor concerns the historical context and controversy of AuEC. The term 'autistic enterocolitis' first introduced by Wakefield et a al. (1998) suggests a contentious association among the MMR vaccine, GI inflammation, and ASD. Their study was later debunked by other studies and officially retracted in 2010 by the Editorial Board of *The Lancet*, where the paper was first published, due to ethical concerns and methodological flaws. In addition, the lead author, Dr Andrew Wakefield lost his medical license to practise in UK. Consequently, the concept of AuEC became highly controversial and widely discredited within the medical community.
- The second factor is tied to the persistent GI issues in ASD. Despite the controversy surrounding the concept of AuEC or the Wakefield paper, many individuals with ASD reportedly experience the four key GI symptoms, i.e., abdominal pain, diarrhea, constipation, and inflammation. As mentioned earlier, several studies have indicated that GI problems are more prevalent in individuals with ASD compared to the typically developed majority in the general population. These GI problems do not result in ASD but should be treated as comorbidities of the disorder. Their symptoms can significantly affect the quality of life and exacerbate behavioral challenges in those with ASD.
- The third factor involves the potential biological links. Findings from emerging research have suggested that there might be biological links between ASD and GI dysfunction. As discussed earlier, some studies have

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identified differences in gut microbiota composition, immune responses, and gut permeability in individuals with ASD. As reported, these findings indicate that GI issues in individuals with ASD might have underlying biological mechanisms that warrant further investigation.

- The fourth factor is related to the holistic understanding and treatment of ASD with GI problems. Re-examining AuEC, real or fictional, can still contribute to a more holistic understanding of ASD, considering both neurological and gastrointestinal aspects. By exploring the potential connections in the G-BA, more comprehensive treatment approaches can be and have already been developed over the time to address both behavioral and GI symptoms. These treatment approaches include dietary interventions, probiotics, or other non-pharmacological therapies (including educational therapy) aimed at improving gut health as well as the overall wellness of an individual.
- The fifth and last factor concerns the scientific rigor and objectivity associated with the Wakefield paper. Revisiting the concept of AuEC with rigorous scientific methods can help disentangle legitimate findings from the discredited claims of the retracted paper. High-quality research can clarify whether there is a distinct GI pathology associated with ASD and, if so, what mechanisms are involved. This objective approach is essential to advancing knowledge and improving care for autistic individuals with GI-related comorbidities.

Finally, despite the controversial origin of AuEC, the authors of this paper strongly believe that re-examining its concept remains crucial for professionals working with autistic clients due to the significant GI issues faced by many of them, the potential biological links, and the opportunity to enhance understanding and treatment of ASD in a holistic manner. By applying rigorous scientific methods, both practitioners and researchers can continue to advance knowledge to improve the quality of life for those affected by ASD and associated GI symptoms.

APPENDIX 1

Phylum Level Differences in Gut Microbiota Composition in Children with ASD

(Iglesias-Vázquez et al., 2020; Zuffa et al., 2023; De Sales-Millán et al., 2024; Levkova et al., 2023; Li et al., 2024)

Micro-organism	Level in ASD	Nature	Associated ASD Symptoms
Actinobacteria (phylum)	Higher	Gram-positive bacteria	GI symptoms, potentially affecting behavior through gut-brain axis (Andreo-Martinez et al., 2019; Nirmalkar et al., 2024)
Akkermansia muciniphila	Lower	Gram-negative anaerobe	Mucin-degrading bacteria; associated with metabolic health. Associated with gut barrier function and metabolism (Glover et al., 2022; Levkova et al., 2023)
Bacteriophages	Altered	Viruses that infect bacteria	May influence bacterial population dynamics (Levkova et al., 2023)
Bacteroides	Mixed results	Gram-negative anaerobes	Dominant in the gut; involved in polysaccharide breakdown; associated with high-fat, animal protein diets. Some species linked to improved neurodevelopment (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Martinez et al., 2022; Nirmalkar et al., 2024)
Bifidobacterium	Lower	Gram-positive anaerobes	Helps in nutrient absorption. Reduced levels may worsen GI and behavioral symptoms (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Martinez et al., 2022; Nirmalkar et al., 2024)
Blautia	Lower	Gram-positive anaerobes	Produce short-chain fatty acids. Part of Firmicutes phylum; involved in nutrient metabolism. Associated with constipation in ASD (Andreo-Martinez et al., 2019; Nirmalkar et al., 2024)
Candida (fungus)	Higher	Eukaryotic fungus	May contribute to GI symptoms and inflammation (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Clostridium	Higher	Gram-positive anaerobes	May produce neurotoxins; linked to GI and behavioral symptoms. Diverse genus; some species are pathogenic (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Glover et al., 2022; Nirmalkar et al., 2024)
Collinsella	Higher	Gram-positive anaerobe	Associated with pro-inflammatory states (Levkova et al., 2023)

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Coprococcus	Lower	Gram-positive anaerobes	Reduced butyrate production; linked to GI issues (Andreo-Martinez et al., 2019; Nirmalkar et al., 2024)
Desulfovibrio	Mixed results	Gram-negative anaerobes	Produces hydrogen sulfide; linked to GI symptoms (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Dialister	Lower	Gram-negative anaerobe	Role in gut health; reduced in ASD (Levkova et al., 2023; Nirmalkar et al., 2024)
Enterobacteriaceae	Mixed results	Gram-negative facultative anaerobes	Potential pathogens; may contribute to inflammation (Andreo-Martinez et al., 2019; Nirmalkar et al., 2024)
Faecalibacterium	Mixed results	Gram-positive anaerobes	Anti-inflammatory effects; reduced in ASD with GI symptoms (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Firmicutes (phylum)	Mixed results	Mostly gram-positive bacteria	Imbalance may affect gut barrier function (Andreo-Martinez et al., 2019; Martinez et al., 2022; Nirmalkar et al., 2024)
Klebsiella	Mixed results	Gram-negative facultative anaerobes	Potential pathogen; may contribute to inflammation (De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Lactobacillus	Mixed results	Gram-positive facultative anaerobes	Helps in digestion, immune function, and pathogen inhibition (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Glover et al., 2022; Nirmalkar et al., 2024)
Methanobrevibacter (Archaea)	Mixed results	Methanogen	Involved in hydrogen metabolism; associated with certain diets. May affect gut transit time and constipation (Levkova et al., 2023)
Parabacteroides	Mixed results	Gram-negative anaerobes	Associated with constipation and GI issues (De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Phascolarctobacterium	Mixed results	Gram-negative anaerobes	Reduced short chain fatty acid production; linked to GI issues (De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Prevotella	Lower	Gram-positive anaerobes	Helps in breaking down complex carbohydrates. Reduced in ASD; linked to diet and GI symptoms (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Glover et al., 2022; Nirmalkar et al., 2024)
Proteobacteria (phylum)	Higher	Mostly gram-negative bacteria	Includes potential pathogens; increased abundance associated with disease states. Indicates dysbiosis; linked to inflammation and GI symptoms (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Martinez et al., 2022; Nirmalkar et al., 2024)
Roseburia	Lower	Gram-positive anaerobe	Butyrate producer; may affect gut inflammation (Levkova et al., 2023; Nirmalkar et al., 2024)
Ruminococcus	Mixed results	Gram-positive anaerobes	Involved in complex carbohydrate breakdown. Some species linked to improved verbal (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Sutterella	Higher	Gram-negative anaerobes	Associated with GI inflammation and symptoms (Andreo-Martinez et al., 2019; De Sales-Millán et al., 2023; Nirmalkar et al., 2024)
Veillonella	Higher	Gram-negative anaerobe	May contribute to gut dysbiosis (Levkova et al., 2023; Nirmalkar et al., 2024)

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