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Gut-brain axis in Attention Deficit Hyperactivity Disorder (ADHD): A narrative review of the links between gut microbiota and ADHD pathophysiology

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A B S T R A C T

Characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity, Attention-Deficit Hyperactivity Disorder (ADHD) is the most prevalent neurodevelopmental disorder, posing a significant public health concern. Its etiopathogenesis is considered multifactorial with complex determinism but remains unclear. Recent research highlights the gut microbiota and the gut-brain axis as promising avenues for understanding and potentially treating ADHD, with a growing number of studies exploring alterations in gut microbiota composition among affected individuals. This narrative review examines the current literature on the role of the gut microbiota in ADHD and focuses on key findings about bacterial composition, how it may be linked to ADHD symptomatology, and the possible mechanisms involved.

While studies consistently report changes in microbial composition and diversity in individuals with ADHD, results remain heterogeneous across taxonomic levels. Some compelling evidence also suggests a link between gut microbial profiles and ADHD symptom severity. The involvement of microbiota in influencing neurodevelopment is proposed to be mediated through mechanisms related to SCFA production, immune modulation, and neurotransmitter synthesis. These findings pave the way for microbiota-targeted interventions as adjunct therapies for ADHD.

This review evaluates areas of consensus and discrepancies between studies, while addressing the methodological limitations present in this field of research. Although the gut microbiota appears to play a meaningful role in the complex and multifactorial origins of ADHD, more rigorous and comprehensive studies are needed to confirm these findings and translate them into effective clinical applications. This could ultimately improve both our understanding and treatment of this heterogeneous disorder.

1. Attention Deficit hyperactivity disorder (ADHD)

1.1. Prevalence and symptomatology

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurodevelopmental disorder in child psychiatry (Polanczyk et al., 2014) with a worldwide prevalence in children and adolescents around 8 % (Ayano et al., 2023; Thomas et al., 2015) and an estimated male-to-female ratio of 2–4:1 (APA, 2013; Bitsko, 2022; Dalsgaard et al., 2020). ADHD is characterized by developmentally inappropriate levels

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of inattention, hyperactivity and impulsivity (APA, 2013). These symptoms negatively affect daily functioning, social interactions, academic performance, as well as physical and mental health (Ayano et al., 2023; Fenollar-Cortés and Fuentes, 2016). Associated with comorbid disorders, such as conduct disorders, anxiety, depression and autism spectrum disorders (ASD), ADHD is actually an undeniable public health priority (Akmatov et al., 2021; Vasileva et al., 2021). ADHD is also associated with a range of executive and attentional deficits (Khaledi et al., 2019; Kofler et al., 2013; Pievsky and McGrath, 2018), predominant in the symptomatology of ADHD associated with structural and functional brain variations (Martella et al., 2020; Samea et al., 2019; Yu et al., 2023). Its symptoms persist into adulthood in 60 % cases and are associated with social and occupational impairment (Sibley et al., 2017).

1.2. Etiology

The etiopathogenesis of ADHD is widely considered multifactorial, arising from complex interactions between genetic and environmental factors (Akutagava-Martins et al., 2016; Faraone et al., 2015). Its etiology remains incompletely understood, suggesting that the factors are interchangeable and no single factor can be identified as an isolated and direct trigger of ADHD. This heterogeneity reflects the phenotypic variability observed in ADHD and continues to hinder diagnosis and treatment (Klein et al., 2019; Thapar et al., 2013). Twin studies consistently demonstrate a genetic contribution, with heritability estimates between 60 % and 90 % (Faraone et al., 2005; Larsson et al., 2014). Large-scale genomic association research (GWAS) identified genes involved in neuronal plasticity and dopaminergic, noradrenergic, and serotonergic systems (Demontis et al., 2019, 2023; Faraone and Larsson, 2019; Franke et al., 2009).

Environmental factors, including prenatal, perinatal, and postnatal conditions (pollutant exposure, psychological stress, …) have been suggested to contribute to ADHD (Kim et al., 2020; Thapar et al., 2013). Their effects, however, appear modest and often intertwined with genetic vulnerability. Individuals genetically predisposed may be more sensitive to specific environmental risks (Dunn et al., 2019; Rutter et al., 2006). Prenatal exposure to certain environmental factors may initiate immune-related processes that interfere with neurodevelopment and increase the risk of ADHD (Razaz and Ananth, 2024). Among these influences, dietary and nutritional factors during gestation and early childhood appear particularly relevant (Lebovitz et al., 2018; Mathee et al., 2020; O'Mahony et al., 2017). Increasing evidence suggests that certain dietary patterns can promote inflammation, oxidative stress, altered gut permeability, changes in microbiome composition, and altered metabolite production, each capable of influencing neurodevelopment (Lebovitz et al., 2018). These findings raise the possibility that gastrointestinal dysregulation contributes to ADHD (Dunn et al., 2019; Verlaet et al., 2014). The gut microbiome may be the missing piece of the neurodevelopmental puzzle, linking early-life stress to brain function and behavior (O'Mahony et al., 2017).

In parallel, accumulating evidence implicates immune-related mechanisms in ADHD pathophysiology. Neuroinflammation, defined as inflammatory activity within neural tissue involving microglia, astrocytes, cytokines, and related molecular processes in the central nervous system (CNS), is now widely considered to be a key factor in ADHD (Dunn et al., 2019; Turiaco et al., 2024). Consistent with this view, ADHD has been linked to elevated inflammatory and immune markers (R.-Y. Zhou et al., 2017), as well as to higher prevalence of immune-related conditions such as eczema, asthma, psoriasis, allergic rhinitis, and type 1 diabetes (Chua et al., 2021; van der Schans et al., 2017). In addition, several susceptibility genes associated with neurodevelopmental risk in ADHD have also been implicated in immune pathways (Chang et al., 2021; Dunn et al., 2019; Leffa et al., 2018; Saccaro et al., 2021; Zayats et al., 2015). These findings support the existence of a pro-inflammatory state in ADHD, which could be a cause, effect, or related phenomenon of the condition (Saccaro et al., 2021).

Immune-related inflammatory processes are consistent with well-established neurobiological models of ADHD that involve dysregulation of the dopaminergic and noradrenergic systems, which underlie impulsivity, behavioral control, and attention (Dunn et al., 2019; Stanford and Sciberras, 2022; Wu et al., 2012). These catecholaminergic pathways are also targeted by ADHD treatments, which modulate catecholamine release and uptake to normalize neurotransmission (Faraone and Glatt, 2009; Verlaet et al., 2018). At the cerebral level, these catecholaminergic disturbances correspond to structural and functional alterations observed in ADHD, suggesting a global delay in brain maturation. These differences include cortical and subcortical activation abnormalities, particularly in prefrontal regions involved in cognitive control, motor planning, and attentional processes (Martella et al., 2020; Samea et al., 2019; Yu et al., 2023).

Recent work has proposed that gut microbes may influence neuroinflammation and catecholamine regulation in reward-related brain regions (Huwart et al., 2025). This suggests a possible connection between diet, the gut microbiome, immune signaling, and neurotransmitter systems relevant to ADHD. Despite ongoing debate, diet has emerged as a relevant area of investigation, with dietary interventions increasingly explored for their potential to alleviate ADHD symptoms, possibly through the modulation of allergic or inflammatory responses that are more prevalent in children with ADHD (Bull-Larsen & Mohajeri, 2019; Lewis et al., 2025; Turiaco et al., 2024). Given the broad influence of the gut on human physiology, and growing evidence that the intestinal microbiota contributes to health across many medical domains (Armour et al., 2019), attention has turned to its communication with the brain. The gut–brain axis, a bidirectional system in which the gut microbiota plays a central role, is now considered a promising framework for understanding neurodevelopment and behavior (Bundgaard-Nielsen et al., 2020; Cryan and Dinan, 2012; McMath et al., 2023; Soltysova et al., 2022). As described in depth in this review, only a handful of studies have investigated the gut-brain axis in ADHD.

2. Gut microbiota and the gut-brain axis

The gut microbiota represents the community of microorganisms including bacteria, viruses, fungi and archaea that are inhabiting the gastrointestinal tract of the host. The term gut microbiome describes the collective genomes of the microorganisms that reside in the gut and the microorganisms themselves. Among these microorganisms, bacteria have been larger investigated whereas more recent research also focused on viruses and fungi. The last estimation evaluated around 3.9×10^{13} the total number of bacteria within human body, a number approximatively equivalent to human eucaryotic cells (Sender et al., 2016). Importantly, these estimates do not consider the viruses and phages also present in our bodies, which could equal the bacterial estimates (Liang and Bushman, 2021).

The interaction between gut bacteria and the host is qualified as a symbiotic relationship since both microbes and the host benefit from this mutually beneficial relationship. Importantly, this host–microbe symbiosis is essential to health and well-being whereas disruption of this symbiotic state, the so-called dysbiosis and transition from symbiosis to dysbiosis have been implicated in human disease (Malard et al., 2021).

Importantly, the gut is also densely innervated by hundreds of millions of neurons that comprise the enteric nervous system (ENS), interacting with the gut microbiota (Geng et al., 2022). This system cooperates with intestinal microbes, intestinal immune system, and endocrine systems to form a complex network that is required to maintain a stable intestinal microenvironment (Geng et al., 2022). Interestingly, the ENS contains integrative neural circuitry with similarities to the CNS of mammals and arising before and independently of the CNS from an evolutionary point of view (Furness and Stebbing, 2018). Therefore, the ENS can be seen as the first brain developed independently of the CNS. Moreover, reciprocal connections between ENS and CNS occur in mammals and are part of the gut-brain axis

(Furness and Stebbing, 2018). For the past two decades there has been growing evidence supporting the roles of gut microbiota as one of the key regulators of gut-brain function which leads to the microbiota gut brain axis concept (Blair et al., 2025). Indeed, bidirectional communications between gut microbes and the brain are supported through the immune system, vagus nerve system, neuroendocrine system, circulatory system and enteric nervous system (Yuan et al., 2023). Specifically, a distinct microbiota-gut-brain axis across the lifespan, especially during neurodevelopment, has been highlighted (Cryan, 2025). In line with this, germ free mice have been reported to present altered neurogenesis processes that are not restored by postweaning microbial colonization (Ogbonnaya et al., 2015). Moreover, a role of the microbiome in neurodevelopmental disorders ranging from ASD to ADHD has also been delineate in animal models (Wright, 1985). Even if this mechanistic perspective should still be supplemented with more translational studies to evaluate the applicability of findings from animal models to human subjects, some preliminary human studies also support a link between gut microbiome and ADHD.

Table 1
Methodological characteristics of the main studies included.

STUDY	YEAR	COUNTRY	SAMPLE ADHD	SAMPLE CTRL	AGE	MEDICATION	DIAGNOSTIC TOOL	MICROBIOTA ANALYSIS
Aarts et al. (2017)	2017	Netherlands	19 ADHD	77 CTRL	ADHD (mean 19,5), CTRL (mean 27,1)	Not mentioned	DSM-IV; K-SADS-PL	16S rRNA
Prehn-Kristensen et al. (2018)	2018	Germany	14 ADHD	17 CTRL	8–15 years	Yes. 10 patients with ADHD had been taking Medikinet or Equasym for more than 1 year. 9/10 interrupted their treatment at least 48 h before the stool collection.	DSM-IV-TR; K-SADS-PL + **Symptoms assessment**: CBCL; ADHD-RS (German version: FBB-HKS)	16S rDNA
Jiang et al. (2018)	2018	China	51 ADHD	32 CTRL	6–10 years	No	DSM-IV; K-SADS-PL + **Symptoms assessment**: CPRS	16S rRNA
L.-J. Wang et al. (2020)	2020	China (Taiwan)	30 ADHD	30 CTRL	6–16 years	No (never)	DSM-IV-TR; K-SADS-E + **Symptoms assessment**: SNAP-IV (parent and teacher form); ADHD-RS	16S rRNA
Wan et al. (2020)	2020	China (Beijing)	17 ADHD	17 CTRL	6–12 years	Not mentioned	DSM-V; K-SADS	Shotgun metagenomics sequencing
Szopinska-Tokov et al. (2020)	2021	Netherlands	41 ADHD	15 subthreshold ADHD and 47 CTRL	ADHD (mean 20,2), CTRL (mean 20,5), Subtrsld (mean 20,2)	Yes. History of ADHD medication.	DSM-IV; K-SADS + **Symptoms assessment**: CAARS; CTRS	16S rRNA
Richarte et al. (2021)	2021	Spain	100 ADHD	100 CTRL	ADULTS (exact age not given)	No	DIVA 2.0; SCID-I and SCID-II + **Symptoms assessment**: ADHD-RS; CFI; WURS; SDS; SCID-I and SCID-II	16S rRNA
G. Zhou et al. (2021)	2021	China	44 ADHD	38 CTRL	6–12 years ADHD (mean 6,5) CTRL (mean 8,6)	Not mentioned	DSM-V	16S rRNA
Lee et al. (2022)	2022	China (Taiwan)	54 ADHD	22 CTRL	6–18 years	No	DSM-V; SNAP IV + **Symptoms assessment**: SNAP-IV; CBCL	16S rRNA
Panpetch et al. (2024)	2024	Thailand	24 ADHD	24 CTRL	6–12 years	No	DSM-V + SNAP IV + **Symptoms assessment**: SNAP-IV	16S rRNA
N. Wang et al. (2024)	2024	China	47 TDAH	60 CTRL	6–16 years	No	DSM-V + K-SADS-PL	Shotgun metagenomics sequencing
Steckler et al. (2024)	2024	Poland/ Israël	42 TDAH	31 CTRL	6–18 years	No	DSM V	16S rRNA + SCFA analysis trough GC-MS

ADHD-RS = the ADHD Rating Scale; CAARS = Conners Adult ADHD Rating Scales; CBCL = Child Behavior Checklist; CGI = the Clinical Global Impression; CPRS = Conners Parent Rating Scales; CTRL = Controls; CTRS = Conners Teacher Rating Scale; DIVA 2.0 = Structured Diagnostic Interview for Adult ADHD; DSM = Diagnostic and Statistical Manual of Mental Disorders; GC-MS = Gas Chromatography-Mass Spectrometry; K-SADS-E = Kiddie Schedule for Affective Disorders and Schizophrenia - Epidemiologic Version; K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia - Present and Lifetime Version; SCFA = Short-Chain Fatty Acid; SCID-I and II = the structured Clinical Interview for DSM-IV Axis I and II Disorders; SDS = Sheehan Disability Inventory; SNAP-IV = Swanson, Nolan, and Pelham-IV Questionnaire; WURS = the Wender Utah Rating Scale.

3. Gut microbiota in ADHD

3.1. State of the art: available studies on gut microbiota in ADHD

Current human studies on gut microbiota in ADHD remain limited but are rapidly increasing, using diverse methodological approaches and research questions. To date, 12 studies have compared the gut microbiota of individuals with ADHD to age-matched controls or unaffected siblings (see Table 1). The majority of these studies involve children and adolescents, although a few have focused on adult patients (Aarts et al., 2017; Richarte et al., 2021; Szopinska-Tokov et al., 2020). In addition, most studies use 16S rRNA sequencing to analyze bacterial populations, with more recent works applying shotgun metagenomics for higher taxonomic resolution (Wan et al., 2020; N. Wang et al., 2024).

ADHD is highly heterogeneous, with substantial variability in symptoms and severity, contributing to inconsistent findings related to gut microbiota. Therefore, rather than solely comparing individuals with ADHD to unaffected controls, investigating gut microbiota variations in relation to symptom profiles may be more informative. Seven clinical studies have examined associations between gut microbiota composition and ADHD symptomatology, assessing how specific taxa or diversity patterns relate to symptom severity. Additional work has linked gut microbiota profiles in ADHD with brain imaging (Aarts et al., 2017) and dietary habits (L.-J. Wang et al., 2020).

Although growing interest, existing studies on the gut microbiota in ADHD show significant methodological variability: from study design and analytical techniques to participant age, geographic location, medication status, and assessment tools. This heterogeneity likely contributes to the inconsistent findings across studies and complicates direct comparisons, as noted in other research contexts (Rodriguez et al., 2024). Table 1 summarizes the key methodological features of the main studies comparing the gut microbiota of individuals with ADHD and control groups, sometimes in relation to symptom severity.

Despite discrepancies, studies report significant microbiota

Table 2
Microbiota diversity and composition in ADHD.

Study	Alpha diversity	Beta diversity	Increasing microbial taxa					Decreasing microbial taxa				
			Phylum	*Order*	*Family*	*Genus*	*Species*	*Phylum*	*Order*	*Family*	*Genus*	*Species*
Aarts et al. 2017	n.s.	n.s.	Actinobacteria	Bifidobacteriales	**Rikenellaceae** Porphyromonadaceae Bifidobacteriaceae	***Bifidobacterium*** *Eggerthella*	***Bacteroides (uniformis, ovatus, vulgatus)*** ***Bifidobacterium (longum, adolescentis, pseudocatenulatum)***	Firmicutes	Clostridiales			
Prehn-Kristensen et al. 2018	↓ in **ADHD** (Shannon index)	**Significant difference**	n.s.	n.m.	Neisseriaceae Bacteroidaceae	*Neisseria*	*n.m.*	n.s.	n.m.			*n.m.*
Jiang et al. 2018	n.s.	n.s.	n.s.	n.m.	Peptostreptococcaceae, Moraxellaceae, Xanthomonadaceae, Peptococcaceae		*n.m.*	n.s.	n.m.	Alcaligenaceae	***Faecalibacterium***, *Lachnoclostridium*, *Sutterella*, ***Dialister***	*n.m.*
Wang et al. 2020	↑ in **ADHD** (Shannon index & Chao 1 index) ↓ in **ADHD** (Simpson index)	n.s.	Fusobacteria	n.m.	n.m.	*Fusobacterium*	***Bacteroides uniformis*** ***Bacteroides ovatus*** *Sutterella stercoricanis*		n.m.	n.m.		***Bacteroides coprocola***
Wan et al. 2020	n.s.	n.s.	n.m.	n.m.	Odoribacteraceae Enterococcaceaeae	*Odoribacter* ***Enterococcus***	***Bacteroides caccae,*** ***Odoribacter splanchnicus,*** *Paraprevotella xylaniphila* *Veillonella parvula*			**Ruminococcaceae**	***Faecalibacterium,*** *Veillonella*	*Faecalibacterium prausnitzii,* *Lachnospiraceae bacterium,* *Ruminococcus gnavus*
Szopinska-Tokov et al. 2021	n.s.	**Significant difference**	n.s.	n.m.		*Ruminoclostridium 9,* ***Ruminococcus2***, ***Clostridiales g,*** *Ruminococcaceae NK4A214 group,* *Ruminococcaceae UCG 003,* *Ruminococcaceae UCG 004,* *Ruminococcaceae UCG 005,* *Ruminococcaceae g-uncultured,* *Family XIII AD3011 group*	*n.m.*	n.s.	n.m.	n.m.		*n.m.*
Richarte et al. 2021	n.s.	n.s.	n.s.	n.m.	Veillonellaceae Selenomonadaceae	***Dialister*** ***Megamonas***	*n.m.*	n.s.	n.m.	Gracilibacteracaea	*Gracilibacter* *Anaerotaenia*	*n.m.*
Zhou et al. 2021	↑ in **ADHD** (Shannon index, Simpson index)	**Significant difference**	n.s.	n.m.	n.m.	***Roseburia*** *Gemmiger* *Acinetobacter* ***Enterococcus*** *Bacteroides* *Streptococcus* ***Faecalibacterium***	*n.s.*	n.s.	n.m.	n.m.	***Bifidobacterium*** *Shigella* *SMB53* *Turicibacter* *Collinsella* ***Ruminococcus*** ***Clostridium***	*n.s.*
Lee et al. 2022	n.s.	**Significant difference**	Proteobacteria	Betaproteobacteriales	Burkholderiaceae	*Agathobacter* *Phascolarctobacterium* *Prevotella_2* ***Acidaminococcus*** ***Roseburia*** ***Ruminococcus gnavus group*** *Parasutterella*	*n.m.*			**Rikenellaceae**	*Alistipes* *Eubacterium eligens group*	*n.m.*
Panpetch et al. 2024	n.s.	n.s.	n.s.	n.m.	n.m.	*Alloprevotella,* *CAG-352,* *Succinivibrio,* ***Acidaminococcus***	*n.m.*	n.s.	n.m.	n.m.	***Megamonas***, *Eubacterium hallii,* *Enterobacter,* *Negativibacillus*	*n.m.*
Wang et al. 2024	↓ in **ADHD** (Shannon index, simpson index)	**Significant difference**	n.m.	n.m.	n.m.	*n.m.*	*Anaerostipes_hadrus,* *Lachnospira,* *Phascolarctobacterium_faecium*	n.m.	n.m.	n.m.	*n.m.*	***Bacteroides_caccae,*** ***Bacteroides_sp_PHL_2737***, ***Odoribacter_splanchnicus,*** *Alistipes_onderdonkii,* *Alistipes_shahii,* *Megamonas_funiformis*
Steckler et al. 2024	↓ in **ADHD** (Shannon index, Observed species, Faith-PD)	n.s.		n.m.	Lachnospiraceae	*Blautia*	*n.m.*	Verrucomicrobia	n.m.	**Ruminococcaceae** Christensenellaceae	*Akkermensia* *Anaerococcus*	*n.m.*

Note. The table presents bacterial taxa whose abundance differs significantly between individuals with ADHD and controls in each included study. Taxa reported as significantly different in at least two independent studies are highlighted in bold. Among these, taxa shown in bold black indicate consistent and replicated findings across studies, whereas taxa shown in bold red reflect divergent or conflicting results.
n.s. = not significant; n.m. = not mentioned; bacteria in plain text = not replicated; bacteria in **bold black** = results replicated by at least two studies; bacteria in **bold red** = results contradicted by at least two studies.

differences between ADHD and controls, suggesting a potential role for the gut microbiota in ADHD pathophysiology. This review synthesizes current findings on bacterial composition, symptom associations, proposed mechanisms, therapeutic implications, and methodological limitations.

3.2. Reported characteristics of the gut microbiota in ADHD case

Modifications of gut microbiota composition among the different comparative clinical studies (ADHD cases versus controls) are summarized in Table 2. The table presents bacterial taxa whose abundance differs significantly between individuals with ADHD and controls in each included study. Bacterial taxa reported as significantly different in at least two independent studies are highlighted in bold. Among these, taxa shown in bold black indicate consistent and replicated findings across studies, whereas taxa shown in bold red reflect divergent or conflicting results between studies.

3.2.1. Alpha diversity

Alpha diversity quantifies microbial richness and/or evenness within a sample using indices such as Shannon, Simpson, Operational Taxonomic Units (OTUs), Observed Species, Chao1, ACE and Faith's PD (Lozupone et al., 2012; The Human Microbiome Project Consortium, 2012).

Case-control studies reporting significant differences generally show reduced alpha diversity in ADHD, though many report no differences (Aarts et al., 2017; Jiang et al., 2018; Lee et al., 2022; Panpetch et al., 2024; Richarte et al., 2021; Szopinska-Tokov et al., 2020; Wan et al., 2020). When differences occur, they typically involve only one or two indices, and indices vary widely across studies, limiting comparability.

Findings also differ between adults and children. Adult microbiota appears neither enriched nor depleted (Aarts et al., 2017; Richarte et al., 2021; Szopinska-Tokov et al., 2020), whereas several child studies report significant differences. Medication may also influence alpha diversity (Sukmajaya et al., 2021; Szopinska-Tokov et al., 2020).

Two meta-analyses yielded inconsistent findings regarding microbial diversity in ADHD (Payen et al., 2022; N. Wang et al., 2022). These studies reported increased alpha diversity in ADHD patients compared to control groups. This finding is unexpected because greater microbial diversity is generally associated with better health (Karkman et al., 2017). More recent analyses, however, found no consistent differences in alpha or beta diversity across age groups (Caputi et al., 2024; Jakobi et al., 2024).

3.2.2. Beta diversity

Beta diversity assesses between-sample differences using metrics such as Bray–Curtis, Jaccard, weighted and unweighted UniFrac (Knight et al., 2018). Five studies report significant ADHD vs control differences in Beta diversity (Lee et al., 2022; Prehn-Kristensen et al., 2018; Szopinska-Tokov et al., 2020; N. Wang et al., 2024; G. Zhou et al., 2021). Szopinska-Tokov et al. (2020) found reduced within-group variability in ADHD, indicating greater homogeneity between members of this group compared to healthy controls group, which may indicate the presence of a bacterial signature related to ADHD (Gkougka et al., 2022). However, other studies found no differences (Jiang et al., 2018; Panpetch et al., 2024; Richarte et al., 2021; Steckler et al., 2024; L.-J. Wang et al., 2020). A meta-analysis in adults reported significant beta diversity differences in three of four studies (Jakobi et al., 2024). Overall, findings on beta diversity remain inconsistent, making it difficult to draw firm conclusions (Gkougka et al., 2022; Shirvani-Rad et al., 2022; N. Wang et al., 2022).

3.2.3. Relative abundance of bacterial taxa in ADHD

Bacteria are classified according to different taxonomic levels: Phylum, Class, Order, Family, Genus and Species, and the results of the studies investigating gut microbiota composition are presented according to this classification. Human gut microbiota is dominated by the phyla Actinobacteria, Proteobacteria, Firmicutes, and Bacteroidetes (Lloyd-Price et al., 2016; The Human Microbiome Project Consortium, 2012), and the same holds for ADHD (Boonchooduang et al., 2020; Caputi et al., 2024). However, even when similar abundances are reported at the phylum level, the composition at the order, family, genus, and species levels can differ considerably between individuals, reflecting substantial heterogeneity (see Table 2) (D'Argenio and Salvatore, 2015; Gkougka et al., 2022; Lozupone et al., 2012).

Meta-analyses show no consistent phylum- or family-level differences (N. Wang et al., 2022). *Blautia* appears to be increased at the genus level, although the available evidence remains limited. Payen et al. (2022) found elevated Actinobacteria Phylum in children with ADHD and highlighted Bifidobacterium as a potential biomarker (Aarts et al., 2017; Bull-Larsen & Mohajeri, 2019).

3.2.4. Association between bacterial profiles and ADHD symptom severity

Several studies have reported associations between ADHD symptom severity and the gut microbiota (Jiang et al., 2018; Panpetch et al., 2024; Prehn-Kristensen et al., 2018; Szopinska-Tokov et al., 2020; L.-J. Wang et al., 2020). These studies have identified specific bacterial genera or species correlated with symptom severity in either inattention and/or hyperactivity/impulsivity, as reported by caregivers (parents and/or teachers) or by the individuals themselves in adult studies. All findings related to the correlation between symptoms and bacterial composition in ADHD studies are summarized in Table 3.

To recapitulate, the study of the links between the gut microbiota and children and adults with ADHD reveals significant correlations with two major bacterial phyla: Bacteroidetes and Firmicutes. One notable result is the inverse relationship between gut bacterial diversity and symptoms of hyperactivity and impulsivity: the less bacterial diversity there is, the more pronounced these symptoms are. Interestingly, in contrast to studies comparing individuals with ADHD to unaffected controls, analyses focusing on correlations between gut bacteria and ADHD symptoms have identified specific taxa showing consistent trends across studies. For example, *CAG-352* is positively correlated with inattention and hyperactivity, while others such as *Eubacterium hallii, Megamonas* and certain *Bacteroides* species show negative correlations with these symptoms.

However, the possibility of obtaining a clear consensus is challenged by individual differences among participants and the diversity of methodological approaches across the different studies. As illustrated in Table 3, the behavior scales used to assess symptom severity vary widely across studies, contributing to substantial heterogeneity. Clinical rating scales are inherently subjective, target different symptom dimensions rely on diverse informants, and use distinct scoring systems. Nevertheless, despite this variability, converging evidence supports the existence of gut–brain communication, with gut microbiota composition potentially modulating ADHD symptoms.

3.2.5. Association between bacterial profiles and brain imaging data

To date, only one study has combined gut microbiome data with brain imaging in adults with ADHD (Aarts et al., 2017). First, it reported that higher levels of *Bifidobacterium* observed in ADHD patients were associated with increased microbial production capacity of the enzyme cyclohexadienyl dehydratase (CDT), an enzyme involved in synthesizing phenylalanine, a dopamine precursor. Second, greater CDT abundance was linked to reduced reward-anticipation activity in the ventral striatum during functional magnetic resonance imaging (fMRI) in ADHD participants. This suggests that gut microbial metabolic pathways may influence dopaminergic signaling in the brain. Overall, the study provides preliminary evidence connecting gut microbiome function with brain reward processing in ADHD (Aarts et al., 2017; Checa-Ros et al., 2021).

Table 3
Reported correlations between gut microbiota and ADHD symptoms.

			SYMPTOMS		
STUDY	SCALES	CORR.	INATTENTION	HYPERACTIVITY/IMPULSVITY	ADHD total
Prehn-Kristensen et al. (2018)	ADHD-RS	+			
		-		Diversity of microbiota	
Jiang et al. (2018)	CPRS	+			
		-		*F Faecalibacterium*	*F Faecalibacterium*
Szopinska-Tokov et al. (2020)	CAARS	+	*F Ruminococcaceae UCG-004*		
	CTRS	-			
L.-J. Wang et al. (2020)	SNAP-IV	+		*B Bacteroides ovatus,* *P Sutterella stercoricanis*	
		-			
Panpetch et al. (2024)	SNAP-IV	+	*B Alloprevotella,* *CAG-352*	*CAG-352*	
		-	*F Eubacterium hallii group,* *F Megamonas,* *F Negativibacillus*	*F Eubacterium hallii group,* *F Megamonas,* *B Butyricimonas*	
ADDITIONAL STUDIES					
Li et al. (2022)	CPRS	+			*B Prevotella buccae,* *A Bifidobacterium breve,* *A Bifidobacterium bifidum*
		-	*B Bacteroides thetaiotaomicron,* *B Bacteroides ovatus*		*B Bacteroides nordii,* *B Bacteroides, cellulosilyticus,* *B Bacteroides intestinalis*
Jakobi et al. (2024) (Meta-analysis)	/	+			*F Eisenbergiella*
		-			

CORR = correlation; (+) = positive correlation; (−) = negative correlation; ADHD-RS = the ADHD Rating Scale; CAARS = Conners Adult ADHD Rating Scales; CPRS = Conners Parent Rating Scales; CTRS = Conners Teacher Rating Scale; SNAP-IV = Swanson, Nolan, and Pelham-IV Questionnaire. A = Actinobacteria; B= Bacteroidetes; F = Firmicutes; P= Proteobacteria.

3.3. Discussion

3.3.1. Key findings in gut microbiota research on ADHD

This review highlights significant differences in gut microbiota composition among individuals with ADHD, in relation to symptom severity. Emerging convergences point to key bacterial functions that may contribute to ADHD pathophysiology, warranting further investigation. Below, we summarize the most consistent findings at the phylum, genus, and species levels.

3.3.1.1. Phylum level. At the phylum level, Firmicutes and Bacteroidetes are frequently reported as significantly increased or decreased in studies comparing the gut microbiota of individuals with ADHD to control groups. Given that these two phyla dominate the human gut microbiota (Mariat et al., 2009), this observation is not trivial. The balance between Firmicutes and Bacteroidetes, commonly operationalized as their ratio (F/B ratio), has been widely studied as an indicator of gut homeostasis and has been implicated in immune, inflammatory, and metabolic regulation (An et al., 2023; Magne et al., 2020; Mariat et al., 2009; Stojanov et al., 2020). Disruptions in this balance have been associated with a range of conditions, including obesity, inflammatory bowel disease, diabetes, cancer, and benign prostatic hyperplasia (An et al., 2023; Magne et al., 2020; Stojanov et al., 2020; Takezawa et al., 2021; Tsai et al., 2021). In neurodevelopmental contexts, an increased F/B ratio has been consistently reported in ASD and linked to microbial metabolites potentially affecting neuronal function and brain development (Houtman et al., 2022; Lacorte et al., 2019; F. Liu et al., 2019; Zhang et al., 2018). Similar alterations, whether driven by reduced Bacteroidetes or increased Firmicutes, may also affect neurodevelopmental trajectories relevant to ADHD (Tamana et al., 2021). Moreover, it has been demonstrated that this ratio naturally changes naturally with age (Mariat et al., 2009; Vaiserman et al., 2020), suggesting that deviations from typical microbial maturation patterns could increase vulnerability to ADHD. Clarifying these associations may improve etiological understanding and inform microbiota-based therapeutic strategies in ADHD (Payen et al., 2022).

3.3.1.2. Genus level

3.3.1.2.1. Bifidobacterium. At the genus level, *Bifidobacterium* (Actinobacteria phylum) appears to be repeatedly associated with ADHD, although findings remain inconsistent (Aarts et al., 2017; Jiang et al., 2018; Li et al., 2022; Pärtty et al., 2015; G. Zhou et al., 2021). This genus is crucial in early development and its concentration naturally declines with age (Aarts et al., 2017; Payen et al., 2022). *Bifidobacterium* has been reported to support intestinal barrier function and immune regulation (Underwood et al., 2015). A longitudinal study showed that infants deficient in *Bifidobacterium* were more likely to develop ADHD later in childhood (Pärtty et al., 2015). Interestingly, it seems that the concentration of *Bifidobacterium* follows an inverse trajectory in ADHD, with marked deficiency in early life followed by predominance during childhood, at the expense of bacteria more suited to development (Aarts et al., 2017; Boonchooduang et al., 2020; Payen et al., 2022). As previously noted, Aarts et al. (2017) showed that variations in *Bifidobacterium* abundance may influence neurodevelopment through pathways related to phenylalanine synthesis and dopaminergic signaling (Bull-Larsen & Mohajeri, 2019; Pärtty et al., 2015; Shirvani-Rad et al., 2022), leading to the proposal that this genus could serve as a marker of ADHD risk (Kalenik et al., 2021; Payen et al., 2022). However, inconsistent findings currently limit its biomarker potential.

In addition, *Bifidobacterium* is known to produce GABA (Sukmajaya et al., 2021), a key inhibitory neurotransmitter in the CNS that has been consistently reported as reduced in ADHD. More recently, two randomized studies with *Bifidobacterium bifidum* Bf-688 supplementation in children with ADHD reported modulation of gut composition, particularly the F/B ratio, and improvements in ADHD symptoms within SNAP-IV scores (L.-J. Wang et al., 2022, 2024). Gastrointestinal symptom improvement with Bf-688 supplementation also indicated better intestinal tolerance and potential metabolic optimization (L.-J. Wang et al., 2024). Although these findings suggest that *Bifidobacterium* may support ADHD treatment via gut–brain axis modulation, the underlying mechanisms remain unclear. Specifically, the roles of GABA and the pathways linking *Bifidobacterium* to symptom changes need further investigation (Dam et al., 2019; Shirvani-Rad et al., 2022; Sukmajaya et al., 2021).

3.3.1.2.2. Ruminococcus. The genus *Ruminococcus* (Firmicutes phylum, Ruminococcaceae family), has also been associated with ADHD, although reported abundance changes remain conflicting (see Tables 2 and 3). Panpetch et al. (2024) further identified increased levels of the Ruminococcaceae genus CAG-352. Ruminococcaceae family is known to be key producers of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate (Qu et al., 2017; Shang et al., 2016; Xie et al., 2022), which maintain gut barrier integrity, modulate immune system, and influence brain function and behavior, suggesting a potential role in ADHD (Dam et al., 2019; Lee et al., 2022; Silva et al., 2020). Interestingly, altered Ruminococcaceae abundance has also been observed across multiple psychiatric conditions (Nguyen et al., 2019; Painold et al., 2019; Rose et al., 2018; L. Wang et al., 2023). In children and adolescents with ADHD, *Ruminococcus gnavus* has been associated with externalizing behaviors such as rule-breaking tendencies and aggression (Lee et al., 2022), potentially mediated by its metabolic products, particularly SCFAs, which influence inflammatory pathways and neurotransmitter systems involved in behavioral regulation.

Several studies report associations between Ruminococcaceae taxa and ADHD symptoms (see Table 3). Szopinska-Tokov et al. (2020) discovered that the sequence of *Ruminococcaceae_UCG_004* matches the species *Eubacterium gabavorous*, the only gut bacteria known to consume GABA. This observation is significant, as GABA functions as a natural inhibitory neurotransmitter that reduces CNS activity by blocking specific brain signals, playing a role in neuropsychiatric disorders, including ADHD (Novell et al., 2020; Schür et al., 2016). Animal studies further support these findings: germ-free mice colonized with ADHD microbiota display anxiety-like behaviors and altered brain structure, with Ruminococcaceae abundance correlating with anxiety (Tengeler et al., 2020). Additional research links Ruminococcaceae to impulsivity, attention deficits, and striatal dopamine receptor alterations in models of addiction and alcoholism (Jadhav et al., 2018; Peterson et al., 2020). These findings converge on SCFAs, GABA metabolism, and dopaminergic systems as possible mechanisms through which Ruminococcaceae may influence ADHD (Steckler et al., 2024).

3.3.1.2.3. Dialister. The genus *Dialister* (Firmicutes phylum) shows variable abundance across studies (see Table 2), being decreased in Jiang et al. (2018) (pediatric study) but increased in Richarte et al. (2021) (adult study). Notably, *Dialister* is also recognized for modulating GABA (F. Liu et al., 2019; Sukmajaya et al., 2021). Jiang et al. (2018) instead propose an inflammatory mechanism, citing evidence that *Dialister* is associated with lower IL-6 levels following a whole-grain diet (Martínez et al., 2013). They noted that the significance of its reduced abundance in ADHD remains unclear but may be related to inflammatory processes and/or dietary factors (Jiang et al., 2018). Additionally *Dialister* may serve as a microbial marker in medicated ADHD patients, as its increase was observed exclusively in medicated groups (Szopinska-Tokov et al., 2020), consistent with its reduction in unmedicated patients (Jiang et al., 2018).

3.3.1.2.4. Faecalibacterium. Faecalibacterium, another Ruminococcaceae genus, also shows contradictory findings. As a key anti-inflammatory genus (Qiu et al., 2013; Quévrain et al., 2016), its reduction is associated with increased pro-inflammatory cytokines (Sukmajaya et al., 2021; Wan et al., 2020), and with asthma, eczema, and allergic rhinitis (Penders et al., 2007), conditions more prevalent in ADHD (Anand et al., 2017; Mitchell and Goldstein, 2014; van der Schans et al., 2017). Reduced *Faecalibacterium* abundance may therefore promote neuroinflammation, affecting microglial activity, synaptic plasticity, and neurogenesis, that may contribute to the development of ADHD (Dunn et al., 2019; Sukmajaya et al., 2021). Wan et al. suggest that reduced *Faecalibacterium*, by promoting a pro-inflammatory state, may contribute to allergy development in ADHD via the gut–brain axis. Because inflammatory cytokines can cross the blood-brain barrier (BBB), they may disrupt neurodevelopment, alter brain function, and affect neurotransmitter release (Wan et al., 2020; Wong et al., 2016). Jiang et al. (2018) similarly reported lower *Faecalibacterium* levels in children with ADHD correlating with greater ADHD severity, consistent with reductions observed in bipolar disorder and depression (Evans et al., 2017; Gkougka et al., 2022; Jiang et al., 2015). These findings reinforce the idea that inflammation, modulated by the gut microbiota, may be a key mechanism in ADHD pathogenesis.

3.3.1.3. Species level. At the species level, several *Bacteroides* taxa (Bacteroidetes phylum) have been implicated in ADHD (Aarts et al., 2017; Wan et al., 2020; L.-J. Wang et al., 2020; N. Wang et al., 2024; G. Zhou et al., 2021). In particular, *Bacteroides uniformis* and *Bacteroides coprocola* were found in higher abundance in children and adults with ADHD (Aarts et al., 2017; L.-J. Wang et al., 2020). These species have been linked to the development of frontal and hippocampal regions, areas showing structural and connectivity alterations in ADHD (McAlonan et al., 2007; Tillisch et al., 2017; Yu et al., 2023). Consistent with these associations, the *Bacteroides* genus correlates positively with hyperactivity and impulsivity ADHD symptoms (Prehn-Kristensen et al., 2018; L.-J. Wang et al., 2020). Although *Bacteroides* species support immune, metabolic, and neurochemical processes by producing vitamins, cofactors, and polysaccharide-degrading enzymes (Sampson and Mazmanian, 2015; Wexler, 2007), they also synthesize amyloids, lipopolysaccharides, enterotoxins, and neurotoxins capable of affecting BBB and CNS integrity (Kitahara et al., 2005; Lukiw, 2016; Prehn-Kristensen et al., 2018). Species such as *B. uniformis*, *B. ovatus*, and *B. coprocola*, involved in nutrient metabolism and plant polysaccharide degradation, were overrepresented in ADHD and may influence the development of brain regions including the frontal lobe, cerebellum, and hippocampus (L.-J. Wang et al., 2020). Moreover, in their pediatric study, Prehn-Kristensen et al. identified two *Bacteroides* operational taxonomic units (OTU_7 and OTU_577) as potential biomarkers for ADHD. These findings further support a complex interaction between the gut microbiota and neurodevelopmental processes relevant to ADHD.

Odoribacter species (Bacteroidetes phylum) have also been reported at higher abundance in both children and adults with ADHD compared to controls (Aarts et al., 2017; Wan et al., 2020). Similar increases have been observed in Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), where this species appears to disrupt dopamine metabolism, suggesting a comparable dopaminergic mechanism in ADHD. *Odoribacter* also produces SCFAs with neuroactive and anti-inflammatory properties (Duan et al., 2020), although elevated SCFA levels have been associated with worsened symptoms in neurodevelopmental disorders such as ASD (Bull-Larsen & Mohajeri, 2019; Srikantha and Mohajeri, 2019). Interestingly, higher *Odoribacter* abundance has likewise been reported in ASD populations (Maini Rekdal et al., 2019; Quagliariello et al., 2018; Srikantha and Mohajeri, 2019). Given the reduced dopaminergic reward system activity characteristic of ADHD (Wan et al., 2020), abnormalities in *Odoribacter* levels may contribute to this dysregulation, supporting its potential role in ADHD pathophysiology.

In conclusion, recent studies on the gut microbiota in ADHD reveal complex mechanisms involving multiple bacterial phyla, genera, and species, each potentially linked to specific functions of the gut-brain axis. Among the key findings, variations in the F/B ratio, the fluctuating abundance of *Bifidobacterium* across the lifespan, and the metabolic roles of bacteria like *Ruminococcus*, *Dialister* and *Odoribacter* emerge as critical elements. These bacteria influence various processes, including neurotransmitter production (dopamine, GABA), inflammatory regulation, and SCFA modulation. Overall, these proposed mechanisms suggest a complex interaction between inflammatory processes, neurochemical functions, and brain development, modulated by gut microbes and potentially contributing to ADHD symptomatology.

3.3.2. Methodological heterogeneity in gut microbiota research on ADHD

Interpreting findings and identifying a bacterial signature for ADHD remain difficult due to substantial methodological heterogeneity across

Table 4
Main sources of bias and variability affecting gut microbiota findings in ADHD studies.

Domain of bias	Source of bias/ heterogeneity	Description and potential impact on results
Population	Sample size	*Small sample sizes, resulting in low statistical power and limited reproducibility.*
	Participant age	*Wide age ranges, despite age-dependent microbiota maturation, limiting biological comparability.*
	Sex ratio	*Markedly imbalanced sex ratios, rarely controlled for, potentially biasing associations.*
	Sampling strategy	*Heterogeneous recruitment sources, introducing selection bias and limiting external validity.*
	Geographic context	*Heterogeneous geographic and cultural settings increasing baseline microbiota variability.*
Clinical characterization	ADHD diagnostic tools	*Heterogeneous diagnostic criteria (different DSM or ICD versions, parent-rated scales, self-report questionnaires), increasing the risk of participant misclassification*
	Assessment of disorder severity	*Inconsistent assessment of ADHD severity using non-uniform, often subjective, tools.*
	Comorbidity assessment	*Insufficient assessment or control of comorbidities, increasing clinical confounding.*
	Control group definition	*Variably defined control groups (healthy volunteers, siblings, occasionally obese individuals), reducing inter-study comparability.*
	Psychotropic medication	*Heterogeneous medication status, insufficiently controlled for microbiota effects.*
Confounding factors	Antibiotic or probiotic use	*Incomplete or inconsistent reporting, leading to major uncontrolled microbiota effects.*
	Dietary patterns	*Diet variably reported or excluded, despite its major influence on gut microbiota.*
	Gastrointestinal disorders	*Inconsistent inclusion or assessment, confounding microbiota–ADHD associations.*
	Other factors	*Key determinants (BMI, early-life factors, lifestyle) rarely documented.*
Biological sampling	Sampling procedures	*Highly heterogeneous collection protocols (home vs clinic, fasting vs postprandial, single vs repeated samples), resulting in substantial pre-analytical variability.*
	Transport and storage conditions	*Variable temperatures and delays before freezing, increasing the risk of bacterial overgrowth or DNA degradation prior to analysis.*
Analytical methods	Techniques used	*Use of diverse analytical approaches (culture-based methods, targeted PCR, RT-PCR, 16S rRNA sequencing, metabolomics, multi-omics), capturing different dimensions of microbiota modulation.*
	DNA extraction	*Different extraction kits and protocols, introducing bias in microbial representation.*
	Targeted 16S region	*Different hypervariable regions sequenced (V1–V2, V3–V4, V6–V8, etc.), limiting taxonomic comparability.*
	Reference databases	*Use of different taxonomic databases (Greengenes, SILVA, RDP, GenBank), leading to non-uniform taxonomic assignment.*
	Bioinformatic pipelines	*Multiple non-standardized bioinformatic workflows, contributing to inconsistent results across studies.*
Statistical analyses	Diversity indices	*Multiple diversity metrics used, with results highly method-dependent.*
	Multiple comparisons	*Limited correction for multiple testing, increasing false-positive risk.*
	Study design	*Exclusively cross-sectional designs, preventing causal inference.*
Interpretation	Definition of dysbiosis	*Lack of a consensual definition of dysbiosis, resulting in conceptual heterogeneity across studies.*
	Technological evolution	*Rapid methodological evolution over time, limiting comparability between earlier and more recent studies.*

studies (see Table 1). Large variations in results relating to microbial composition, diversity indices and clinical associations reflect inconsistent study designs and the sensitivity of microbiota analyses. Table 4 summarizes the main sources of methodological bias and heterogeneity, together with their potential impact on results reported in the scientific literature concerning the gut microbiota in pediatric and adult ADHD.

Population characteristics, including sample size, age distribution, sex ratio, sampling strategy, and geographic context may significantly influence results, as these factors can affect microbial profiles (Lacorte et al., 2019). Regarding age distribution, the current literature is largely dominated by studies in children and adolescents, whereas data in adults remain limited, complicating comparisons. Studies indicate that gut microbiota profiles associated with ADHD may vary across developmental stages, and that age may represent an important contextual factor when interpreting microbiota-related findings. Consequently, lifespan-oriented approaches, including longitudinal designs are recommended to better account for age-related variability in gut microbiota findings in ADHD.

Medication status is another critical factor: reduced alpha diversity and shifts in genera such as *Dialister* have been observed in patients taking medication (Prehn-Kristensen et al., 2018; Szopinska-Tokov et al., 2020). Therefore, medication could alter microbial composition and represents a significant factor that must be considered, emphasizing the importance of stratifying participants based on their exposure to treatment.

Inclusion and exclusion criteria also differ greatly across studies, especially regarding antibiotic or probiotic use, prematurity, and mode of birth, all major determinants of microbiota composition that are not consistently controlled (Shirvani-Rad et al., 2022). For example, the early use of antibiotics, which are known to disrupt the gut microbiota, has been directly associated with a higher risk of developing ADHD (Slykerman et al., 2019).

Diagnostic inconsistency adds further complexity: studies employ different DSM or ICD versions, rarely independently validating diagnoses, and often apply distinct tools to cases and controls (Lacorte et al., 2019). Furthermore, ADHD severity and comorbidities, which are common in neurodevelopmental disorders, are often underreported (Jurek et al., 2021). These disparities increase the risk of bias and complicate the establishment of reliable correlations between the microbiota and ADHD symptoms.

The studies mentioned below primarily explored the gut-brain axis using clinical questionnaires, which are subjective tools susceptible to biases related to respondents and observation conditions (Power et al., 1998; Tripp et al., 2006). It is likely that evaluating bidirectional interactions between ADHD clinical manifestations and the gut microbiota using behavioral scales alone does not provide sufficiently specific and objective insights into these relationships. Cognitive deficits, particularly in executive and attentional domains, are well-documented as central to ADHD (Pievsky and McGrath, 2018), yet they are not fully accounted for in these approaches. To date, no study has investigated the relationship between gut microbiota composition and cognitive performance assessed using standardized neuropsychological tests in ADHD subjects compared to typically developing individuals. Incorporating such measures alongside established clinical questionnaires could provide more precise and mechanistically informative insights into gut–-brain interactions by enabling directly quantifiable assessments of symptom severity and more detailed characterization of individual cognitive profiles, thereby enhancing the interpretability and translational relevance of future findings.

Additionally, confounding factors such as diet, physical activity, and sociocultural influences are inconsistently controlled across studies. Specific diets are associated with the abundance of certain bacterial genes (Rojo-Marticella et al., 2022), making dietary patterns and nutrient intake crucial factors in microbiota studies, as they can strongly impact results. Furthermore, differences in technical methods and analysis, including DNA extraction, sequencing platforms, bioinformatic pipelines, sampling, transport, and storage, hinder comparability (Hiergeist et al., 2020; Jurek et al., 2021).

However, in their meta-analysis, N. Wang et al. (2022) evaluated the quality of all included studies on gut microbiota and ADHD using the Newcastle-Ottawa Scale (NOS) and found that all included studies were of high methodological quality. Suggesting that the lack of replicability and consensus in this field is more likely due to significant methodological variability across studies rather than a deficiency in methodological quality.

To address current challenges in ADHD microbiota research, several complementary strategies can be considered (Hiergeist et al., 2020; Jurek et al., 2021). These include the standardization of protocols for sampling, DNA analysis, and sequencing, as well as the implementation of multicenter longitudinal studies to better assess potential causal relationships between the gut microbiota and ADHD. Adopting a lifespan-oriented perspective that integrates children, adolescents, and adults may help account for age-related changes in gut microbiota. In addition, integrative multi-omics approaches combining microbiota data with metabolomics, transcriptomics, and proteomics, together with standardized neuropsychological assessments, could enhance the robustness, interpretability, and reproducibility of gut–brain association studies in ADHD.

4. Conclusion and therapeutic prospects

This review highlights the growing body of evidence suggesting a complex interplay between the gut microbiota and ADHD in pediatric and adult populations. Current studies point to alterations in microbiome composition and diversity in individuals with ADHD, with significant yet inconsistent findings across phyla, genera, and species levels. The involvement of key bacterial taxa, such as those within the Firmicutes and Bacteroidetes phyla, underscores the potential role of microbiota in influencing neurodevelopment through mechanisms like SCFA production, modulation of inflammation, and neurotransmitter synthesis (Aarts et al., 2017; Jiang et al., 2018; Panpetch et al., 2024). However, methodological variability has made it difficult to identify a definitive microbial signature for ADHD.

These studies carry important implications. However, most of the available evidence remains correlational and does not permit causal inferences. The findings nonetheless support the exploration of microbiota-targeted interventions as potential adjunctive therapies for ADHD. Importantly, well-designed and adequately controlled intervention trials are required before any clinical recommendations can be made. Accumulating evidence suggests that gut microbiota modulation may influence neurodevelopmental and behavioral outcomes, thereby offering a potential complement to standard pharmacological treatments (Allahyari et al., 2024; Kalenik et al., 2021). Probiotics have received increasing attention. *Lactobacillus rhamnosus GG* has demonstrated beneficial effects on emotional regulation and cognitive function, potentially via the GABAergic system through the vagus nerve (Bravo et al., 2011; Kalenik et al., 2021; Pärtty et al., 2015; Rianda et al., 2019). Similarly, *Bifidobacterium bifidum* supplementation has been linked to reductions in hyperactivity and impulsivity, as well as favorable changes in gut microbial composition in patients with ADHD (Y. Liu et al., 2025; L.-J. Wang et al., 2022, 2024). Moreover, combining probiotic supplements with pharmacological treatments such as methylphenidate (MPH) appears to enhance symptom reduction in certain studies (Allahyari et al., 2024; Ghanaatgar et al., 2023).

In parallel, dietary interventions involving prebiotics have also gained attention. Diets low in processed foods and rich in fiber, fruits, vegetables, and polyphenols, such as Mediterranean or vegetarian patterns, has been linked to a lower risk of ADHD and less severe symptoms (Darzi et al., 2022; Park et al., 2012; San Mauro Martín et al., 2018). Polyphenols exert antioxidant and anti-inflammatory effects, with compounds like Pycnogenol® showing efficacy in reducing inattention and hyperactivity (Darzi et al., 2022; Luyens et al., 2024; Turiaco et al., 2024; Verlaet et al., 2018). Although preliminary data are encouraging, further research is needed to confirm these findings and establish evidence-based recommendations, provided that causal relationships and clinically meaningful effect sizes can be demonstrated, potentially paving the way for more targeted and personalized ADHD management.

Future work should employ longitudinal designs to map microbiota development and integrate metagenomics, metabolomics, neuroimaging, and cognitive assessment to clarify gut–brain mechanisms, thereby paving the way for innovative diagnostic and therapeutic strategies (Gkougka et al., 2022). In conclusion, while the gut microbiota emerges as a compelling factor in the multifactorial etiology of ADHD, more robust and integrative studies are essential to translate these findings into clinical applications, ultimately improving the management and understanding of this complex and heterogeneous disorder.

CRediT authorship contribution statement

Barbara Luyens: Writing – original draft, Writing - review & editing, Methodology, Investigation, Data curation. **Francisco Felgueroso-Bueno:** Writing – review & editing. **Amandine Everard:** Writing – original draft, Writing – review & editing. **Isabelle Massat:** Writing – review & editing.

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Declaration of competing interest

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