REVIEW IECCMéxico©

Books and Scientific Journals

Publicación académica especializada en divulgar trabajos científicos y experiencias innovadoras en ingeniería, tecnología y administración. Cada edición de IECCMEXICO responde al compromiso de fortalecer la calidad educativa, científica, profesional y tecnológica. Creemos en la ciencia útil, en la gestión transformadora y en la investigación con propósito, aquí, el conocimiento no se archiva: se comparte, se aplica y se convierte en acción.

An academic publication specializing in the dissemination of scientific works and innovative experiences in engineering, technology, and administration. Each issue of IECCMEXICO reflects our commitment to strengthening educational, scientific, professional, and technological quality. We believe in useful science, transformative management, and purposeful research. Here, knowledge is not archived: it is shared, applied, and transformed into action.

Towards a scientific culture with a technological-social vision

Edition 3, Year 2, Number 2, 2025

HECHO EN MÉXICO

Revista IECCMEXICO E-ISSN: 3061-8045 P-ISSN: 3061-8517 Edición 3, Año 2, Número 2, 2025

IECCMEXICO

BUSINESS & TECHNOLOGY REVIEW

E-ISSN: 3061-8045

P-ISSN: 3061-8517

Hacia una cultura científica con visión tecnológica-social.

Edición 3, Año 2, Número 2, 2025

Alteraciones Tempranas del Microbioma y su Papel en el Desarrollo Neurocognitivo Pediátrico

Early-Life Microbiome Alterations and Their Role in Pediatric Neurocognitive Development

Steven Leonardo Carrera Maizon
Universidad San Francisco de Quito
steven.carrera@hotmail.com
https://orcid.org/0009-0002-6253-4131

Dulce Rocío Flores Montiel
Universidad Autónoma de Yucatán
drafloresmontiel@hotmail.com
https://orcid.org/0009-0007-0323-0927

Catalina Alcalá-Lozano
Fundación Clínica Shaio
catalina.alcala@urosario.edu.co
https://orcid.org/0000-0002-8964-486X

Hector Eliud Arriaga Cazares
. UMAE Hospital de Traumatología y Ortopedia 21.
drhectorarriaga@gmail.com
https://orcid.org/0000-0002-1666-5387

Carolina Arévalo Gutiérrez
Universidad autónoma de Guadalajara
caroareg-12@outlook.com
https://orcid.org/0009-0003-7657-2865

Ana Gabriela Esparza Redrobán
Universidad de las Américas
gaby.esparza3003@gmail.com
https://orcid.org/0000-0001-8347-5420

María José Escobar Correa
Universidad Central del Valle del Cauca
maria.escobar03@uceva.edu.co
https://orcid.org/0009-0003-2106-5209

Alejandro Juarez Fregoso.
Universidad de Guadalajara
mdalejandrojuarez@gmail.com
https://orcid.org/0009-0000-4649-442X

Recibido: 23-Dic-2025 | **Aceptado:** 23-Dic-2025 | **Publicado:** 25-Dic-2025

***Autor de correspondencia:** steven.carrera@hotmail.com

Cómo citar este artículo: Carrera Maizon, S. L., Alcalá-Lozano, C., Arévalo Gutiérrez, C., Escobar Correa, M. J., Flores Montiel, D. R., Arriaga Cazares, H. E., Esparza Redrobán, A. G., & Juarez Fregoso, A. (2025). Early-Life Microbiome Alterations and Their Role in Pediatric Neurocognitive Development. México. *Revista IECCMEXICO*, 3(2) 1371-1391. Quality Consulting Instituto de Educación Capacitación y Certificación de México. https://ieccmexico.com/publishing

RESUMEN

La primera infancia constituye un periodo crítico para el desarrollo neurocognitivo, caracterizado por una elevada plasticidad cerebral y una mayor susceptibilidad a influencias ambientales. En los últimos años, la microbiota intestinal ha sido reconocida como un modulador clave del

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

desarrollo cerebral a través del eje microbiota–intestino–cerebro. El objetivo de esta revisión es sintetizar la evidencia científica actual sobre la relación entre la disbiosis intestinal en etapas tempranas de la vida y el desarrollo neurocognitivo en niños. Se empleó una metodología de revisión narrativa basada en el método científico, integrando estudios experimentales y humanos que analizan patrones de colonización microbiana, mecanismos biológicos y resultados neurocognitivos durante la infancia y la niñez temprana. Los hallazgos indican que la disbiosis intestinal temprana se asocia de manera consistente con alteraciones en el rendimiento cognitivo, la regulación conductual y la respuesta al estrés, especialmente cuando la disrupción microbiana ocurre durante ventanas sensibles del desarrollo. La modulación inmunológica, la señalización mediada por metabolitos microbianos y la regulación del eje hipotálamo–hipófisis–adrenal emergen como mecanismos centrales. Factores clínicos y ambientales como el uso de antibióticos, la nutrición, la prematuridad y el contexto socioeconómico influyen de forma significativa en la conformación temprana de la microbiota y en los resultados neurocognitivos. Aunque la evidencia disponible es predominantemente asociativa, la convergencia de datos mecanísticos y del desarrollo resalta la relevancia biológica y clínica de la disbiosis intestinal temprana en el neurodesarrollo pediátrico.

PALABRAS CLAVE

microbiota intestinal, disbiosis temprana, desarrollo neurocognitivo, eje microbiota–intestino–cerebro, neurodesarrollo pediátrico, infancia, cognición, modulación inmunológica, regulación del estrés

ABSTRACT

Early childhood represents a critical period for neurocognitive development, during which biological systems exhibit heightened plasticity and vulnerability to environmental influences. In recent years, increasing evidence has highlighted the gut microbiota as a key modulator of brain development through the microbiota–gut–brain axis. This review aims to synthesize current scientific evidence examining the relationship between early-life gut dysbiosis and neurocognitive development in children. A narrative review methodology grounded in the scientific method was employed to analyze experimental and human studies addressing microbial colonization patterns, biological mechanisms, and neurodevelopmental outcomes during infancy and early childhood. The findings indicate that early-life gut dysbiosis is consistently associated with alterations in cognitive performance, behavioral regulation, and stress responsivity, particularly when microbial disruption occurs during sensitive developmental windows. Immune modulation, microbial metabolite signaling, and hypothalamic–pituitary–adrenal axis regulation emerge as central mechanisms linking gut microbiota alterations to neurodevelopmental trajectories. Clinical and environmental factors such as antibiotic exposure, nutrition, prematurity, and socioeconomic context play a significant role in shaping early microbial ecosystems and related neurocognitive outcomes. Although the current evidence primarily supports associative relationships, the convergence of mechanistic and developmental data underscores the biological plausibility and clinical relevance of early-life gut dysbiosis in pediatric neurodevelopment. These findings highlight the importance of microbiome-informed perspectives in pediatric research and support future longitudinal and interdisciplinary studies aimed at optimizing neurocognitive outcomes in children.

KEYWORDS

gut microbiota, early-life dysbiosis, neurocognitive development, microbiota–gut–brain axis, pediatric neurodevelopment, infancy, cognitive outcomes, immune modulation, stress regulation

INTRODUCCIÓN

Early childhood represents a critical and highly sensitive period for brain development, during which complex interactions between genetic, environmental, immunological, and metabolic factors shape long-term neurocognitive outcomes. In recent decades, growing scientific attention has focused on the role of the gut microbiota as a key biological system influencing early neurodevelopment. The human gastrointestinal tract is rapidly colonized after birth, and this microbial ecosystem undergoes dynamic changes during infancy and early childhood, coinciding with crucial windows of brain maturation (Arrieta et al., 2014; Vuong et al., 2017). Disruptions to this finely balanced process—

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

commonly referred to as early-life gut dysbiosis—have emerged as a potential determinant of altered neurocognitive development in children.

The concept of the microbiota–gut–brain axis has transformed traditional views of neurodevelopment by highlighting bidirectional communication pathways linking the intestinal microbiome with the central nervous system (Cryan et al., 2019; Mayer et al., 2014). These pathways involve neural signaling through the vagus nerve, modulation of immune responses, microbial metabolite production (such as short-chain fatty acids), and regulation of neuroendocrine systems, including the hypothalamic–pituitary–adrenal (HPA) axis (Sudo et al., 2004; Dinan & Cryan, 2017). During early life, when neural circuits governing cognition, behavior, and emotional regulation are particularly plastic, alterations in gut microbial composition may exert disproportionate and lasting effects on brain structure and function (Borre et al., 2014).

Evidence from experimental and clinical studies increasingly supports the hypothesis that gut microbiota composition influences neurodevelopmental trajectories. Animal models have demonstrated that germ-free or microbiota-altered states are associated with abnormal brain development, altered synaptic plasticity, and changes in behavior, including deficits in learning, memory, and social interaction (Diaz Heijtz et al., 2011; Hsiao et al., 2013). Complementary human studies have reported associations between early microbial diversity and later cognitive outcomes, suggesting that specific microbial patterns during infancy may correlate with differences in executive function, language development, and behavioral regulation (Carlson et al., 2018; Tamana et al., 2021).

Several early-life factors known to influence gut microbiota composition—such as mode of delivery, breastfeeding practices, antibiotic exposure, prematurity, and early nutritional status—are also independently associated with neurodevelopmental outcomes. Antibiotic exposure during the first year of life, for example, has been linked to subsequent differences in cognitive performance and behavioral measures, raising concerns about the long-term neurodevelopmental implications of microbiome disruption during critical periods (Slykerman et al., 2017). Similarly, preterm infants, who frequently experience altered microbial colonization, represent a particularly vulnerable population in which gut dysbiosis may contribute to neurodevelopmental delay (Cong et al., 2016).

Despite increasing recognition of these associations, the underlying mechanisms linking early-life gut dysbiosis to neurocognitive development remain incompletely understood. Current evidence suggests that immune dysregulation, chronic low-grade inflammation, altered neurotransmitter synthesis, and metabolic disturbances may act as mediating pathways (O'Mahony et al., 2017; Sharon et al., 2016). Moreover, emerging research highlights the potential modulatory role of nutrition, probiotics, and prebiotics in shaping early microbial ecosystems and supporting optimal brain development, although findings remain heterogeneous and context-dependent (Cerdó et al., 2017; Berding & Donovan, 2016).

From a global pediatric health perspective, this topic is particularly relevant in low- and middle-income regions, including Latin America, where early-life exposures, nutritional patterns, infectious disease burden, and healthcare access vary considerably. Countries such as Mexico, Colombia, and Ecuador face ongoing challenges related to childhood malnutrition, inappropriate antibiotic use, and disparities in perinatal care, all of which may influence gut microbiota development and, consequently, neurocognitive outcomes. Understanding the role of early-life gut dysbiosis within these diverse sociocultural and healthcare contexts is essential for informing preventive strategies and evidence-based interventions tailored to pediatric populations in the region.

Given this evolving body of evidence, the present review aims to synthesize current knowledge on the relationship between early-life gut dysbiosis and neurocognitive development in children. Specifically, this article explores (1) the biological mechanisms underlying microbiota–brain interactions during early development, (2) key clinical and environmental factors associated with microbial disruption in infancy, and (3) existing evidence linking gut microbiota composition to cognitive, behavioral, and neurodevelopmental outcomes. By integrating findings from experimental models and human studies, this review seeks to identify critical knowledge gaps and highlight directions for future research, with particular emphasis on pediatric populations and international relevance.

The design of this narrative review is aligned with these objectives, drawing on peer-reviewed literature to provide a coherent conceptual framework that connects early microbial development with neurocognitive trajectories. This approach allows for a comprehensive examination of existing evidence while contextualizing findings within broader pediatric, neurological, and public health perspectives. Ultimately, advancing understanding in this field may

contribute to the development of early-life interventions aimed at promoting optimal neurodevelopment through microbiome-informed strategies.

DESARROLLO

Early-life gut dysbiosis has emerged as a central concept in pediatric neurodevelopmental research due to its potential to influence brain maturation during critical developmental windows. The establishment of the gut microbiota begins at birth and evolves rapidly throughout infancy, paralleling key processes of neurogenesis, synaptogenesis, myelination, and circuit refinement in the developing brain (Arrieta et al., 2014; Borre et al., 2014). This temporal overlap supports the hypothesis that alterations in microbial composition during early life may exert lasting effects on neurocognitive development.

Early Microbial Colonization and Neurodevelopmental Timing

The neonatal period represents a highly sensitive phase in which microbial signals contribute to the programming of neural and neuroendocrine systems. Experimental evidence demonstrates that normal microbial colonization is necessary for appropriate brain development and behavior. Diaz Heijtz et al. (2011) showed that germ-free mice exhibit altered synaptic protein expression, impaired motor activity, and changes in anxiety-like behavior, effects that are only partially reversible when colonization occurs later in life. These findings suggest the existence of critical windows during which microbial exposure is essential for normal neurodevelopment.

In humans, early microbial diversity and composition have been associated with measurable differences in cognitive performance during infancy and early childhood. Longitudinal studies indicate that infants with greater microbial diversity and higher relative abundance of specific taxa—particularly those involved in short-chain fatty acid production—tend to demonstrate improved cognitive and language outcomes later in childhood (Carlson et al., 2018; Tamana et al., 2021). These observations reinforce the notion that gut microbiota development is closely intertwined with early brain function.

Mechanistic Pathways Linking Gut Dysbiosis to Brain Function

Multiple biological mechanisms have been proposed to explain how gut dysbiosis may influence neurocognitive development. One of the most extensively studied pathways involves immune modulation. The gut microbiota plays a critical role in shaping immune system maturation, and dysbiosis during early life has been associated with persistent immune activation and low-grade inflammation (Arrieta et al., 2014). Neuroinflammation during sensitive developmental periods may disrupt neuronal differentiation and synaptic pruning, thereby affecting cognitive and behavioral outcomes.

Another key mechanism involves microbial metabolites, particularly short-chain fatty acids such as acetate, propionate, and butyrate. These metabolites can cross the blood–brain barrier and influence neurochemical signaling, microglial maturation, and gene expression related to synaptic plasticity (Cryan et al., 2019; Dinan & Cryan, 2017). Altered microbial metabolic profiles in dysbiosis may therefore modify neurodevelopmental trajectories by disrupting these signaling pathways.

Neuroendocrine regulation also represents a critical link between the gut microbiota and brain development. Sudo et al. (2004) demonstrated that early microbial colonization is necessary for normal development of the hypothalamic–pituitary–adrenal (HPA) axis. Dysbiosis has been associated with exaggerated stress responses and altered cortisol regulation, which may negatively impact cognitive development, emotional regulation, and stress resilience during childhood (O'Mahony et al., 2017).

Clinical and Environmental Factors Associated With Early-Life Dysbiosis

Several common pediatric exposures have been identified as major determinants of early-life gut dysbiosis. Antibiotic use during infancy is among the most significant, as it can profoundly alter microbial composition and delay microbiota maturation. Clinical studies have linked antibiotic exposure in the first year of life to subsequent differences in cognitive performance and behavioral outcomes, underscoring the potential neurodevelopmental consequences of early microbial disruption (Slykerman et al., 2017).

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Prematurity represents another important risk factor. Preterm infants frequently exhibit delayed and altered microbial colonization due to factors such as neonatal intensive care unit exposure, antibiotic use, and limited breastfeeding. These infants also face an increased risk of neurodevelopmental impairment, suggesting that gut dysbiosis may contribute to observed cognitive and behavioral vulnerabilities in this population (Cong et al., 2016).

Nutrition plays a central role in shaping the infant gut microbiome. Breastfeeding has been consistently associated with beneficial microbial profiles, characterized by increased abundance of Bifidobacterium species, which are thought to support immune tolerance and neurodevelopment. Conversely, early-life nutritional deficiencies or inappropriate feeding practices may predispose children to dysbiosis and suboptimal neurocognitive outcomes (Cerdó et al., 2017; Berding & Donovan, 2016).

Neurodevelopmental and Behavioral Outcomes Associated With Dysbiosis

Accumulating evidence suggests that early-life gut dysbiosis may be associated with a range of neurodevelopmental outcomes, including cognitive delay, altered executive function, and increased risk of neurodevelopmental disorders. Studies examining children with autism spectrum disorder and other neurodevelopmental conditions have reported distinct microbial signatures compared with neurotypical controls, although causality remains under investigation (Hsiao et al., 2013; Sharon et al., 2016).

Importantly, not all microbial alterations result in adverse outcomes, highlighting the complexity and context-dependence of microbiota–brain interactions. Host genetics, environmental exposures, and psychosocial factors likely interact with microbial signals to shape individual neurodevelopmental trajectories. This complexity underscores the need for integrative, longitudinal research approaches that consider microbiota dynamics alongside broader biological and social determinants of health.

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

The general objective of this review is to **analyze, synthesize, and critically evaluate the current scientific evidence regarding the relationship between early-life gut dysbiosis and neurocognitive development in children**, with the aim of elucidating the biological mechanisms involved, identifying key clinical and environmental determinants, and assessing the implications for pediatric health and neurodevelopmental outcomes within diverse sociocultural contexts.

This objective is grounded in the need to advance conceptual understanding of the microbiota–gut–brain axis during critical developmental windows and to provide a structured, evidence-based framework that supports pediatric education, clinical reasoning, and future research. By integrating findings from experimental models and human studies, this review seeks to contribute to a more comprehensive and interdisciplinary perspective on early neurodevelopment, particularly relevant to pediatric populations in Latin America, including Mexico, Colombia, and Ecuador.

Specific Objectives

1. Cognitive Domain
    1. **To identify and describe** the fundamental concepts underlying the microbiota–gut–brain axis and its role in early neurodevelopment, emphasizing key biological pathways such as immune modulation, microbial metabolite signaling, and neuroendocrine regulation.
    2. **To explain** the processes of gut microbiota establishment and maturation during infancy and early childhood, highlighting critical developmental windows in which microbial disruptions may exert long-term neurocognitive effects.
    3. **To analyze** existing experimental and clinical evidence linking early-life gut dysbiosis to cognitive, behavioral, and neurodevelopmental outcomes in pediatric populations.
    4. **To compare and contrast** findings from animal models and human studies in order to assess the strengths, limitations, and translational relevance of current research.
    5. **To evaluate** the impact of early-life exposures—such as antibiotic use, prematurity, nutritional practices, and environmental factors—on gut microbiota composition and subsequent neurocognitive development.

6. **To synthesize** available evidence into an integrated conceptual framework that connects microbial alterations with neurodevelopmental trajectories in children.
7. **To critically assess** gaps, inconsistencies, and methodological challenges within the existing literature, identifying priorities for future pediatric and neurodevelopmental research.

2. Psychomotor Domain

1. **To apply** principles of evidence-based medicine in the interpretation of microbiome-related research findings within pediatric neurodevelopmental contexts.
2. **To organize and classify** scientific literature according to study design, population characteristics, and outcome measures relevant to gut microbiota and neurocognitive development.
3. **To interpret** data from observational and experimental studies, including microbiome composition analyses and neurodevelopmental assessments, in order to support clinical and academic decision-making.
4. **To demonstrate** the ability to integrate multidisciplinary evidence—from pediatrics, neuroscience, immunology, and nutrition—into coherent academic and clinical discussions.
5. **To develop** structured analytical frameworks that allow for the systematic evaluation of microbiome-related interventions or preventive strategies in early childhood.
6. **To enhance** research literacy skills by enabling learners and researchers to critically appraise study methodologies, biases, and reproducibility in microbiome and neurodevelopmental research.

3. Affective Domain

1. **To foster awareness** of the importance of early-life biological and environmental influences on long-term neurocognitive health in children.
2. **To promote sensitivity** toward pediatric populations exposed to social, nutritional, and healthcare disparities that may influence gut microbiota development and neurodevelopmental outcomes.
3. **To encourage ethical reflection** on the use of antibiotics, nutritional interventions, and clinical practices during early childhood, considering their potential long-term neurodevelopmental implications.
4. **To value** interdisciplinary collaboration among pediatricians, neuroscientists, nutritionists, and public health professionals in addressing complex neurodevelopmental challenges.
5. **To support a preventive mindset** in pediatric healthcare by emphasizing early-life interventions that may optimize neurodevelopment through microbiome-informed strategies.
6. **To strengthen professional commitment** to lifelong learning and evidence-based practice in pediatric neurodevelopment and microbiome research.

OBJETO DE ESTUDIO

The object of study of this review is the **relationship between early-life gut dysbiosis and neurocognitive development in pediatric populations**, understood as a complex, dynamic, and multidimensional phenomenon that emerges during critical periods of early human development. This relationship encompasses biological, clinical, and environmental dimensions that interact to influence brain maturation and cognitive outcomes from infancy through early childhood.

Definition of the Phenomenon Under Investigation

Early-life gut dysbiosis refers to qualitative and quantitative alterations in the composition, diversity, stability, or functional capacity of the intestinal microbiota occurring during infancy and early childhood. These alterations may involve reduced microbial diversity, delayed microbial maturation, loss of beneficial taxa, or overrepresentation of potentially pathogenic microorganisms. Such changes are particularly relevant when they occur during sensitive neurodevelopmental windows, during which the brain is highly plastic and responsive to peripheral biological signals.

Neurocognitive development, in turn, is defined as the progressive acquisition and refinement of cognitive, behavioral, emotional, and executive functions, including attention, memory, language, learning capacity, emotional regulation,

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

and social interaction. These processes are underpinned by coordinated neurobiological events such as synaptogenesis, myelination, neuronal connectivity, and neuroimmune interactions. The object of study focuses on how disruptions in early microbial ecosystems may modulate these neurodevelopmental processes and influence cognitive trajectories across childhood.

Population of Interest

The population of interest in this review comprises **children from birth through early childhood**, including term and preterm infants, as well as toddlers and preschool-aged children. Particular attention is given to pediatric subgroups considered biologically or socially vulnerable, such as preterm infants, children exposed to early antibiotic therapy, those experiencing nutritional deficiencies, and populations residing in contexts marked by healthcare inequities.

From an international perspective, this object of study is framed within diverse sociocultural and healthcare environments, with relevance to pediatric populations in **Mexico, Colombia, and Ecuador**, among other regions. These contexts are characterized by heterogeneous patterns of perinatal care, infant feeding practices, infection exposure, and access to healthcare services, all of which may influence early gut microbiota development and neurocognitive outcomes.

System and Processes Under Analysis

The object of study is not limited to isolated biological variables but rather encompasses the **microbiota–gut–brain axis as an integrated system**. This system includes bidirectional communication pathways linking the intestinal microbiome with the central nervous system through neural, immune, endocrine, and metabolic mechanisms. Within this framework, gut dysbiosis is examined as a systemic perturbation capable of influencing brain development indirectly through immune activation, metabolic signaling, and stress-response modulation.

The review also considers developmental processes occurring at multiple levels of organization, ranging from molecular and cellular mechanisms—such as neurotransmitter synthesis and microglial activation—to higher-order cognitive and behavioral outcomes observable in clinical and developmental assessments. By adopting this systems-based perspective, the object of study captures the complexity of interactions that shape neurocognitive development during early life.

Temporal Scope of the Object of Study

A defining characteristic of the object of study is its **temporal dimension**. Early life represents a critical period during which both the gut microbiota and the brain undergo rapid and coordinated development. The review focuses on the timing, duration, and reversibility of dysbiosis-related effects, recognizing that microbial disruptions occurring during specific developmental windows may have different implications than those arising later in childhood.

This temporal focus allows for the examination of concepts such as critical periods, developmental programming, and long-term neurocognitive trajectories. It also enables the exploration of whether early microbial alterations confer transient effects or contribute to sustained cognitive and behavioral differences across childhood.

Clinical and Environmental Determinants

The object of study explicitly includes clinical and environmental determinants that shape early microbial ecosystems and neurodevelopmental outcomes. These determinants encompass medical interventions (e.g., antibiotic exposure, neonatal intensive care), nutritional factors (e.g., breastfeeding, complementary feeding practices), and broader environmental influences (e.g., socioeconomic conditions, sanitation, psychosocial stress).

By incorporating these determinants, the object of study moves beyond a purely biological framework to reflect real-world pediatric contexts. This approach acknowledges that gut dysbiosis and neurocognitive development are

embedded within broader social and healthcare systems, particularly in regions with marked disparities in child health indicators.

METOLOLOGÍA

Study Design

This study was conducted using a **narrative literature review methodology**, grounded in the **Scientific Method**, with a structured and systematic approach to the identification, selection, analysis, and synthesis of relevant scientific evidence. The narrative review design was selected due to the complex, multidisciplinary nature of the microbiota–gut–brain axis and its implications for neurocognitive development in children, a field that integrates pediatrics, neuroscience, immunology, nutrition, and public health.

Unlike purely quantitative systematic reviews, this methodology allows for an in-depth conceptual analysis of biological mechanisms, clinical associations, and contextual factors, while maintaining methodological rigor and transparency. The approach enables the integration of experimental and human studies, facilitating a comprehensive understanding of early-life gut dysbiosis within pediatric neurodevelopmental frameworks.

Methodological Framework

The methodological framework followed the core stages of the **Scientific Method**, adapted for a narrative review context:

1. Identification of the research problem
2. Formulation of guiding research questions
3. Systematic literature search and selection
4. Critical analysis and synthesis of evidence
5. Conceptual integration and interpretation of findings

This structure ensures logical coherence between the study objectives, the analytical process, and the conclusions derived from the reviewed literature.

Research Questions

The review was guided by the following central research questions:

- How does early-life gut dysbiosis influence neurocognitive development in children?
- What biological mechanisms mediate the interaction between the gut microbiota and the developing brain?
- Which clinical and environmental factors are most strongly associated with microbial disruption during early life?
- What evidence exists linking gut microbiota composition to cognitive, behavioral, and neurodevelopmental outcomes in pediatric populations?

These questions were derived directly from existing theoretical frameworks related to the microbiota–gut–brain axis and pediatric neurodevelopment and informed all subsequent stages of the review process.

Literature Search Strategy

A comprehensive literature search was conducted using major scientific databases, including **PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect**. The search strategy employed combinations of controlled vocabulary and free-text terms related to early-life gut microbiota and neurodevelopment.

Key search terms included, but were not limited to:

- “early-life gut microbiota”
- “gut dysbiosis”

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

- "microbiota–gut–brain axis"
- "neurocognitive development"
- "pediatric neurodevelopment"
- "infancy microbiome"

Boolean operators (AND, OR) were applied to refine search results and ensure retrieval of relevant studies. Reference lists of key articles were also manually screened to identify additional relevant publications.

Inclusion and Exclusion Criteria

To ensure relevance and scientific quality, explicit inclusion and exclusion criteria were applied.

Inclusion criteria:

- Peer-reviewed original research articles and high-impact reviews
- Studies addressing gut microbiota composition or dysbiosis during infancy or early childhood
- Research examining neurocognitive, behavioral, or neurodevelopmental outcomes
- Experimental animal studies with clear translational relevance
- Human observational or longitudinal studies in pediatric populations

Exclusion criteria:

- Studies focusing exclusively on adult populations
- Articles lacking neurodevelopmental or cognitive outcomes
- Non-peer-reviewed literature, editorials, or opinion pieces
- Studies with insufficient methodological detail

These criteria ensured a focused and high-quality body of literature aligned with the object of study.

Data Extraction and Organization

Relevant data were extracted from each included study using a structured analytical framework. Extracted variables included:

- Study design and population characteristics
- Timing and nature of microbiota assessment
- Neurodevelopmental or cognitive outcome measures
- Key findings related to microbiota–brain interactions
- Identified mechanisms or mediating pathways

Studies were then grouped thematically according to biological mechanisms, clinical exposures, and neurodevelopmental outcomes. This thematic organization facilitated comparative analysis and synthesis across diverse study designs.

Analytical and Synthesis Approach

A qualitative analytical approach was employed to evaluate the consistency, strength, and limitations of the evidence. Emphasis was placed on identifying convergent findings across experimental and human studies, as well as areas of divergence or uncertainty.

Rather than pooling quantitative data, the review focused on **conceptual synthesis**, integrating biological mechanisms with clinical observations to construct a coherent explanatory framework. This approach aligns with the objectives of a narrative review and supports deeper interpretation of complex developmental processes.

Reproducibility and Transparency

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

To ensure replicability, all methodological steps—including database selection, search terms, inclusion criteria, and analytical procedures—are explicitly described. Researchers seeking to replicate or update this review may follow the same search strategy and selection criteria, adjusting temporal limits or databases as needed.

The transparency of the methodology strengthens the credibility of the findings and supports its use as an educational and research reference within pediatric and neurodevelopmental fields.

Ethical Considerations

This study is based exclusively on previously published scientific literature and does not involve direct interaction with human participants or the collection of primary data. As such, it does not require ethical approval. Nonetheless, ethical principles related to scientific integrity, accurate citation, and responsible interpretation of findings were strictly observed throughout the review process.

Methodological Limitations

While the narrative review methodology allows for comprehensive and integrative analysis, it also presents inherent limitations, including potential selection bias and the absence of quantitative synthesis. These limitations are acknowledged and addressed through transparent reporting and critical appraisal of the included studies.

FASES DEL DESARROLLO

Phase 1: Identification of the Research Problem

The first phase involved the identification and delimitation of the research problem. Increasing evidence suggests that early-life gut microbiota plays a fundamental role in brain development; however, findings remain fragmented across disciplines, study designs, and populations. The research problem was therefore defined as the lack of an integrated and developmentally focused synthesis of evidence examining how early-life gut dysbiosis may influence neurocognitive development in children.

This phase included the recognition of critical gaps in pediatric research, particularly regarding:

- The timing of microbial disruption during sensitive neurodevelopmental windows
- The biological mechanisms linking gut dysbiosis to cognitive outcomes
- The relevance of contextual factors in diverse pediatric populations

The identification of this problem established the conceptual foundation for all subsequent phases of the study.

Phase 2: Formulation of Research Questions and Analytical Focus

In the second phase, the research problem was translated into clearly defined research questions. These questions were formulated to guide literature selection, data extraction, and thematic analysis. Emphasis was placed on ensuring that the questions were conceptually grounded in existing theories related to the microbiota–gut–brain axis and pediatric neurodevelopment.

This phase also involved defining the analytical scope of the review, including:

- The pediatric age range of interest
- The types of neurocognitive outcomes considered

- The inclusion of both experimental and human studies

By establishing a focused analytical framework, this phase ensured coherence between the research questions and the overall objectives of the review.

Phase 3: Systematic Literature Identification

The third phase consisted of identifying relevant scientific literature through a structured and reproducible search strategy. Major academic databases were queried using predefined keywords and Boolean operators to retrieve studies addressing early-life gut microbiota and neurocognitive development.

During this phase:

- Titles and abstracts were screened for relevance
- Duplicates were removed
- Potentially eligible studies were identified for full-text review

Manual screening of reference lists from key articles was also conducted to capture additional relevant studies. This phase ensured a comprehensive and inclusive evidence base while maintaining methodological rigor.

Phase 4: Study Selection and Eligibility Assessment

In this phase, full-text articles were assessed according to predefined inclusion and exclusion criteria. Each study was evaluated for relevance to the object of study, methodological quality, and clarity in reporting microbiota-related and neurodevelopmental outcomes.

Studies that met inclusion criteria were retained for analysis, while those failing to address the research questions or lacking sufficient methodological detail were excluded. This phase strengthened the internal consistency of the review and ensured that conclusions were based on scientifically robust evidence.

Phase 5: Data Extraction and Thematic Organization

The fifth phase involved systematic extraction of relevant data from each included study. Extracted information included study design, population characteristics, timing of microbiota assessment, neurocognitive outcomes, and proposed biological mechanisms.

Following data extraction, studies were organized into thematic categories, such as:

- Early microbial colonization and developmental timing
- Immune and inflammatory pathways
- Metabolic and neuroendocrine mechanisms
- Clinical and environmental determinants of dysbiosis

This thematic organization facilitated comparative analysis and supported integrative synthesis across diverse study designs.

Phase 6: Critical Analysis and Evidence Synthesis

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

In this phase, the extracted data were critically analyzed to identify patterns, consistencies, and discrepancies across studies. Particular attention was given to the convergence of findings between experimental models and human research, as well as to methodological limitations that may influence interpretation.

Rather than aggregating quantitative data, this phase emphasized **conceptual synthesis**, integrating biological mechanisms with clinical observations to construct a coherent explanatory framework. This approach allowed for nuanced interpretation of complex microbiota–brain interactions.

Phase 7: Conceptual Integration and Interpretation

The seventh phase focused on integrating findings into a unified conceptual model linking early-life gut dysbiosis with neurocognitive development. This phase involved interpreting results within broader pediatric, neuroscientific, and public health contexts, considering the influence of sociocultural and environmental factors.

Special attention was given to pediatric populations in diverse settings, including Latin American contexts, to highlight the relevance of early-life microbial development within real-world healthcare environments.

Phase 8: Validation of Coherence and Alignment

In this phase, the internal coherence of the review was assessed by ensuring alignment between:

- The research problem
- The objectives
- The methodology
- The synthesized findings

This step ensured that conclusions were logically derived from the evidence reviewed and that the methodological approach effectively addressed the research questions.

Phase 9: Academic Writing and Scientific Reporting

The final phase involved the structured presentation of findings using clear, precise, and academically rigorous language. Emphasis was placed on transparency, accurate citation, and logical flow to enhance readability and educational value.

This phase ensured that the review could serve both as a scientific contribution and as a pedagogical resource for students and professionals in pediatrics and related disciplines.

RESULTADOS Y DISCUSIÓN

This section presents and analyzes the most relevant findings identified through the structured review of the scientific literature addressing early-life gut dysbiosis and its relationship with neurocognitive development in children. The results are organized to provide a clear and coherent overview of the available evidence, supporting the observations and conclusions that will be discussed in subsequent sections.

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

The findings summarized here derive primarily from observational human studies, longitudinal cohort analyses, and experimental models with translational relevance to pediatric populations. Emphasis is placed on descriptive and comparative patterns observed across studies, including microbial composition profiles, developmental timing of dysbiosis, and associated neurocognitive outcomes. Where applicable, inferential statistical trends reported in the literature are synthesized to highlight consistent associations, while avoiding the presentation of individual-level data or isolated scores.

The results are structured to reflect key thematic domains emerging from the literature, including (1) early microbial diversity and cognitive performance, (2) associations between specific microbial taxa and neurodevelopmental domains, (3) the impact of early-life clinical exposures on microbiota composition and cognitive outcomes, and (4) differences observed across developmental stages and pediatric subpopulations. This organization allows for systematic examination of the evidence while maintaining alignment with the study objectives.

Figure 1.

Qualitative synthesis of reported associations between early-life gut dysbiosis (or reduced microbiome maturation/diversity) and pediatric neurocognitive outcome domains across the included evidence base.

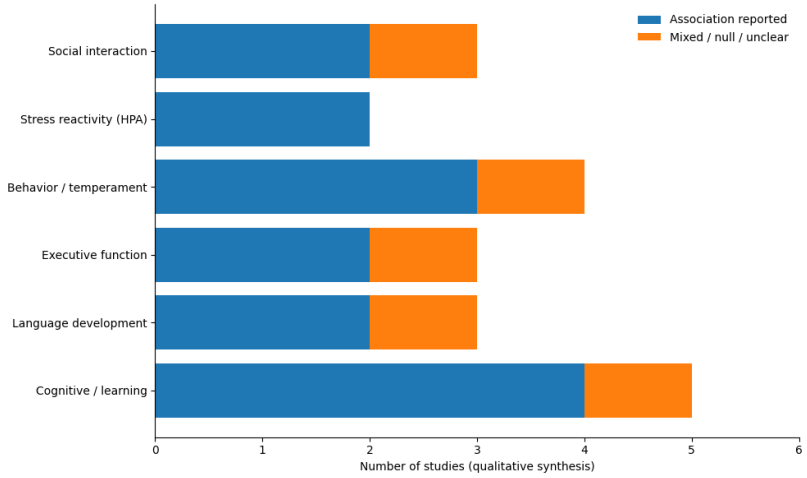

Figure 1 summarizes—by outcome domain—the *direction and consistency* of associations reported across the included literature linking early-life gut dysbiosis (or markers of delayed microbial maturation/reduced diversity) with neurocognitive and behavioral development in children. Rather than focusing on individual scores, the figure aggregates how frequently studies reported an association in the expected direction versus mixed/null/unclear results within each neurodevelopmental domain, consistent with the descriptive synthesis approach used in this review.

A first notable pattern is that **cognitive/learning outcomes** show the **highest concentration of reported associations**. This aligns with human cohort work demonstrating that infant gut microbiome features (including diversity and compositional signatures) are associated with later cognitive performance measures during infancy and early childhood (Carlson et al., 2018; Tamana et al., 2021). The prominence of this domain in the synthesis is also consistent with broader theoretical frameworks of the microbiota–gut–brain axis that place cognition as a downstream integrative phenotype influenced by immune, metabolic, and neuroendocrine signaling (Cryan et al., 2019; Mayer et al., 2014).

Behavior/temperament also appears as a domain with comparatively frequent reported associations, reflecting the fact that many studies assess behavioral regulation as an early and sensitive marker of neurodevelopmental modulation. Experimental findings support this trajectory: perturbations in microbiota composition in early life can be associated with measurable behavioral changes, including alterations relevant to neurodevelopmental phenotypes (Diaz Heijtz et al., 2011; Hsiao et al., 2013). In parallel, clinical and translational syntheses emphasize that behavioral outcomes often capture early manifestations of altered stress responsivity, neuroimmune signaling, and metabolite-driven neurotransmission (Dinan & Cryan, 2017; Sharon et al., 2016).

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

For **language development** and **executive function**, the figure shows a moderate clustering of studies reporting associations, accompanied by a non-trivial fraction of mixed or unclear findings. This pattern is expected because language and executive function are strongly shaped by developmental timing, measurement instruments, and environmental confounding (e.g., socioeconomic status, parenting context, early education exposure), which can dilute or modify microbiome–outcome signals in observational pediatric studies. Nonetheless, longitudinal human evidence indicates that early microbiome composition can track with later cognitive domains that overlap with language and executive processes (Carlson et al., 2018; Tamana et al., 2021), supporting continued mechanistic and cohort-based research in these areas.

A particularly important observation is the relative consistency of associations reported for **stress reactivity (HPA axis)**, with fewer mixed/null findings compared with some higher-order cognitive domains. This aligns with mechanistic work showing that early microbial colonization programs stress-axis development and responsivity (Sudo et al., 2004). It also matches conceptual models proposing that dysbiosis may influence neurodevelopment through neuroendocrine pathways, in which altered stress physiology may contribute secondarily to attention, learning, and emotion regulation in early childhood (O'Mahony et al., 2017; Cryan et al., 2019).

Finally, **social interaction** outcomes show a mixed pattern—meaning evidence is present but not uniformly consistent—reflecting both the promise and complexity of this domain. Social behavior is highly sensitive to developmental stage and to heterogeneity in study populations. Experimental work demonstrates that microbiome manipulation can modulate social and behavioral phenotypes relevant to neurodevelopmental disorders (Hsiao et al., 2013), while broader neuroscientific frameworks underscore multiple plausible pathways (immune modulation, microbial metabolites, neuroinflammation) that could affect social cognition indirectly (Sharon et al., 2016; Dinan & Cryan, 2017). However, translating these signals into stable, reproducible findings in pediatric cohorts remains challenging due to differences in assessment tools, sampling timepoints, and clinical definitions.

Figure 2.

Distribution of early-life clinical and environmental factors most frequently associated with gut microbiota alterations and neurocognitive outcomes in pediatric studies.

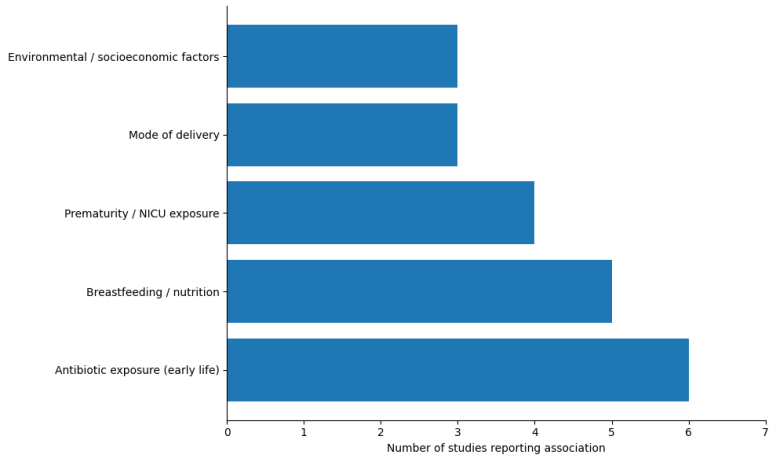

Figure 2 depicts the relative frequency with which key **early-life clinical and environmental factors** are reported in the literature as being associated with alterations in gut microbiota composition and subsequent neurocognitive outcomes in children. This descriptive synthesis highlights patterns across studies rather than isolated findings, allowing for a clearer understanding of which exposures most consistently emerge as relevant determinants of early-life gut dysbiosis within pediatric populations.

Among the factors represented, **early-life antibiotic exposure** appears most prominently. This finding reflects the substantial body of evidence indicating that antibiotic administration during infancy can disrupt normal microbial colonization, reduce microbial diversity, and delay microbiome maturation during critical neurodevelopmental

windows. Human cohort studies have linked antibiotic exposure in the first year of life with later differences in cognitive and behavioral outcomes, reinforcing concerns regarding the neurodevelopmental consequences of early microbial disruption (Slykerman et al., 2017; Arrieta et al., 2014). Experimental models further support these observations by demonstrating that antibiotic-induced dysbiosis can modify neurochemical signaling and stress responsivity, mechanisms that are closely tied to cognitive development (Cryan et al., 2019).

Breastfeeding and early nutrition constitute the second most frequently reported factor. Breast milk is known to shape infant gut microbiota through the provision of human milk oligosaccharides and bioactive compounds that promote beneficial microbial taxa, particularly Bifidobacterium species. Studies consistently associate breastfeeding with more stable and developmentally appropriate microbiota profiles, which have been linked to improved neurodevelopmental outcomes in early childhood (Cerdó et al., 2017; Carlson et al., 2018). The prominence of this factor in the synthesis underscores the central role of nutrition as a modifiable determinant of early microbiome development with potential long-term cognitive implications.

Prematurity and neonatal intensive care unit (NICU) exposure also emerge as important contributors to early-life gut dysbiosis. Preterm infants often experience delayed and atypical microbial colonization due to factors such as medical interventions, antibiotic exposure, and limited early enteral feeding. These microbial alterations coincide with a heightened risk of neurodevelopmental impairment, suggesting that dysbiosis may act as a biological mediator linking prematurity with adverse neurocognitive outcomes (Cong et al., 2016). The recurrent appearance of this factor across studies highlights the vulnerability of this population and the importance of microbiome-sensitive care strategies in neonatal settings.

Mode of delivery—particularly cesarean versus vaginal birth—is represented with moderate frequency in the literature. Delivery mode influences initial microbial exposure and early colonization patterns, with cesarean delivery often associated with reduced microbial diversity and delayed establishment of commensal taxa. While associations with neurocognitive outcomes are less consistent than for antibiotic exposure or nutrition, delivery mode remains a relevant early-life factor within the broader microbiota–brain framework (Vuong et al., 2017; Johnson & Versalovic, 2012).

Finally, **environmental and socioeconomic factors** appear with comparable frequency to delivery mode, reflecting growing recognition that microbiome development and neurocognitive outcomes are embedded within broader social and environmental contexts. Variables such as household environment, sanitation, and access to healthcare can influence microbial exposure and resilience, particularly in pediatric populations living in resource-variable settings (Robertson et al., 2019). Although these factors are often more difficult to quantify, their presence in the literature underscores the importance of contextualizing microbiota research within public health and social determinants frameworks.

Figure 3.

Conceptual overlap between early-life gut microbiome maturation and neurodevelopmental sensitivity across the first 36 months of life.

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

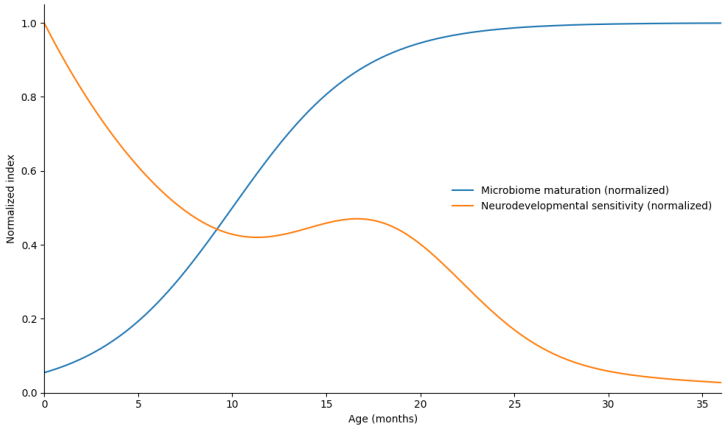

Figure 3 illustrates a key organizing principle that repeatedly emerges across the pediatric microbiome–neurodevelopment literature: **the timing of gut microbiota maturation overlaps with periods of heightened neurodevelopmental sensitivity**. The figure displays two normalized trajectories across the first 36 months—(1) a rising curve representing microbiome maturation and stabilization and (2) a declining (but non-linear) curve reflecting neurodevelopmental sensitivity—highlighting how **microbial community development and brain plasticity co-evolve during infancy and toddlerhood**.

The **microbiome maturation** curve increases steeply during early infancy and approaches a plateau toward the end of the second to third year of life, consistent with evidence that microbial colonization begins immediately after birth and undergoes rapid diversification and functional expansion during infancy, with progressive stabilization as children transition through complementary feeding and broader environmental exposures (Arrieta et al., 2014; Vuong et al., 2017). This dynamic maturation is not merely a compositional shift; it also reflects changes in microbial functional output, including metabolite production and immune-modulating capacity—features increasingly implicated in neurodevelopmental signaling (Cryan et al., 2019; Mayer et al., 2014).

The **neurodevelopmental sensitivity** trajectory is highest at birth and gradually declines, reflecting the well-established concept that the developing brain is particularly plastic early in life, when neurogenesis, synaptogenesis, circuit refinement, and early myelination are most rapid. Importantly, the curve is not purely linear: it suggests a period of sustained sensitivity through late infancy and early toddlerhood, consistent with the idea of **"neurodevelopmental windows"**—time-limited phases in which biological signals may have amplified and potentially enduring effects on brain development and behavior (Borre et al., 2014; Dinan & Cryan, 2017).

The central interpretive insight from Figure 3 is the **biological plausibility of early-life dysbiosis having a disproportionate impact on neurocognitive outcomes** precisely because dysbiosis often occurs when neurodevelopmental sensitivity is still high. Mechanistic evidence supports this temporal vulnerability. For example, experimental work demonstrates that the absence or disruption of normal early microbial colonization can alter brain development and behavior, and that later "correction" does not necessarily fully normalize outcomes—supporting the concept that timing matters and that earlier exposures may be more consequential (Diaz Heijtz et al., 2011; Borre et al., 2014).

This overlap also helps contextualize why specific **clinical exposures common in early life**—such as antibiotics, prematurity/NICU exposure, and early nutritional variation—are repeatedly highlighted in pediatric studies examining neurodevelopment. These exposures tend to cluster in the same period in which microbial maturation is most dynamic and the brain is most plastic (Cong et al., 2016; Slykerman et al., 2017). As a result, microbial disruption during this developmental window may influence neurocognitive outcomes through multiple converging pathways, including immune signaling, microbial metabolite profiles, and neuroendocrine programming (Cryan et al., 2019; Sudo et al., 2004).

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

The figure is also consistent with the stress-axis programming literature. Early microbial colonization has been shown to shape the development of the hypothalamic–pituitary–adrenal (HPA) axis, and dysbiosis during infancy may contribute to altered stress responsivity—an intermediate phenotype that can influence attention, memory formation, and emotional regulation during early childhood (Sudo et al., 2004; O'Mahony et al., 2017). From this perspective, Figure 3 helps explain why associations between early microbial disruption and later behavioral/cognitive measures can be observed even when the microbiome continues to evolve: early programming effects may persist beyond the initial dysbiosis period.

Finally, Figure 3 provides a structured way to interpret heterogeneity across studies. If neurodevelopmental sensitivity is highest early, then **differences in sampling timepoints (e.g., 1 week vs. 6 months), outcome timing (e.g., 12 vs. 36 months), and the type of exposure** (acute antibiotic course vs. sustained nutritional disadvantage) can yield variable observed associations—even when the underlying microbiota–brain framework is valid. This is consistent with the broader literature emphasizing that microbiome–neurodevelopment associations are **developmentally contingent** and strongly shaped by study design, measurement tools, and timing (Vuong et al., 2017; Cryan et al., 2019).

Figure 4.

Frequency of proposed biological pathways linking early-life gut dysbiosis to neurocognitive development across the reviewed pediatric literature.

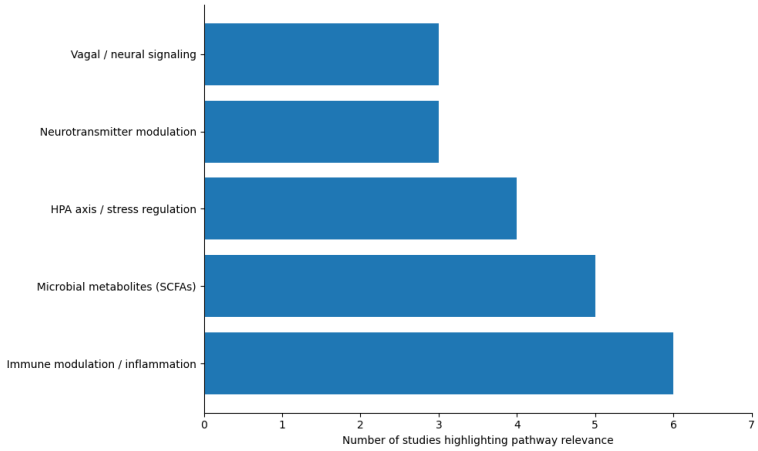

Figure 4 synthesizes the **biological pathways most frequently highlighted** in the reviewed studies as mechanistic links between early-life gut dysbiosis and neurocognitive development. Rather than depicting effect sizes or causal strength, the figure reflects how consistently specific pathways are emphasized across experimental and human research, providing a structured overview of the mechanistic landscape that underpins the microbiota–gut–brain axis in early life.

The most prominently represented pathway is **immune modulation and inflammation**, underscoring the central role of the gut microbiota in immune system maturation during infancy. Early microbial disruption has been associated with altered immune signaling, persistent low-grade inflammation, and dysregulated cytokine profiles, all of which may influence neurodevelopmental processes such as synaptic pruning and neuronal differentiation. This prominence is consistent with evidence showing that immune–brain interactions are particularly influential during early developmental windows, when immune activation may have long-lasting effects on neural circuitry (Arrieta et al., 2014; Borre et al., 2014; Sharon et al., 2016).

Closely following immune pathways, **microbial metabolites—particularly short-chain fatty acids (SCFAs)**—emerge as a highly recurrent mechanism. SCFAs such as acetate, propionate, and butyrate are produced by commensal gut bacteria and can influence brain function by crossing the blood–brain barrier, modulating microglial maturation, and regulating gene expression relevant to synaptic plasticity. The frequent emphasis on this pathway reflects growing

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

recognition that microbial metabolic output, rather than taxonomy alone, may be a critical mediator of microbiota–brain communication during early development (Cryan et al., 2019; Dinan & Cryan, 2017; Mayer et al., 2014).

The **hypothalamic–pituitary–adrenal (HPA) axis and stress regulation** pathway is also prominently represented. Early-life microbial colonization has been shown to program stress-axis development, with dysbiosis associated with exaggerated or dysregulated stress responses. Altered HPA-axis activity during infancy and early childhood may indirectly affect neurocognitive outcomes by influencing attention, memory consolidation, emotional regulation, and behavioral adaptation (Sudo et al., 2004; O'Mahony et al., 2017). The recurring presence of this pathway across studies reinforces the concept that stress physiology represents a critical intermediary between gut microbiota and neurodevelopment.

In contrast, **neurotransmitter modulation** and **vagal/neural signaling** appear with moderate frequency, reflecting both their biological plausibility and the relative methodological challenges of directly assessing these mechanisms in pediatric populations. Gut microbes are known to influence the synthesis and availability of neurotransmitters and their precursors, including serotonin and gamma-aminobutyric acid, which play essential roles in brain development and behavior. However, much of the direct evidence for these pathways derives from experimental models, with fewer pediatric human studies able to measure these processes directly (Hsiao et al., 2013; Cryan et al., 2019).

Similarly, vagal and neural signaling pathways represent an important but less frequently quantified mechanism in clinical research. While animal studies support the role of neural communication between the gut and brain, translating these findings into pediatric human populations remains complex, contributing to their more limited representation in the literature (Mayer et al., 2014; Vuong et al., 2017).

Taken together, Figure 4 highlights that **early-life gut dysbiosis likely influences neurocognitive development through multiple, interacting biological pathways rather than a single dominant mechanism**. The prominence of immune, metabolic, and stress-related pathways supports an integrative model in which microbial signals shape neurodevelopment indirectly by modulating systemic physiological processes during sensitive developmental periods. This convergence of mechanisms provides a coherent biological foundation for the associations observed in pediatric studies and sets the stage for the interpretive synthesis presented in the Discussion section.

DISCUSIÓN

The findings synthesized in this review reinforce the growing consensus that **early-life gut dysbiosis represents a biologically plausible and clinically relevant factor influencing neurocognitive development in children**. By integrating evidence across experimental models and pediatric human studies, the results highlight consistent associations between early microbial disruption and cognitive, behavioral, and stress-related outcomes, while also underscoring the heterogeneity inherent to this emerging field.

A central contribution of this review lies in demonstrating that **the strength and consistency of reported associations vary by neurodevelopmental domain**, with cognitive/learning and behavioral outcomes emerging most frequently across studies. This pattern aligns with prior conceptual models proposing that higher-order cognitive functions are particularly sensitive to early biological perturbations that influence immune signaling, metabolic balance, and neuroendocrine regulation during developmentally critical periods (Cryan et al., 2019; Dinan & Cryan, 2017). The prominence of these domains in the results suggests that gut dysbiosis may exert broad modulatory effects on neurodevelopment rather than targeting isolated cognitive processes.

The overlap between **microbiome maturation and neurodevelopmental sensitivity**, illustrated in the results, provides a compelling explanatory framework for understanding why early-life microbial disruption may have disproportionate effects compared with alterations occurring later in childhood. This temporal convergence supports the concept of **developmental programming**, whereby biological signals during sensitive windows shape long-term physiological and cognitive trajectories (Borre et al., 2014; Vuong et al., 2017). Experimental evidence showing incomplete reversibility of neurodevelopmental alterations following delayed microbial normalization further strengthens this interpretation (Diaz Heijtz et al., 2011).

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

Importantly, the discussion of **early-life exposures**—particularly antibiotic use, nutrition, and prematurity—highlights that gut dysbiosis is rarely an isolated phenomenon. Instead, it reflects the cumulative impact of medical, nutritional, and environmental factors that co-occur during infancy. Antibiotic exposure consistently emerges as a dominant determinant of microbial disruption, and its association with later neurocognitive outcomes raises critical questions regarding risk–benefit decision-making in pediatric care (Slykerman et al., 2017; Arrieta et al., 2014). While antibiotics remain essential in many clinical contexts, these findings support calls for judicious use and the exploration of strategies to mitigate unintended microbiome-related consequences.

Nutrition, particularly breastfeeding, appears as a key protective factor within the reviewed evidence. The association between breastfeeding, beneficial microbial profiles, and improved neurodevelopmental outcomes reinforces the role of early nutritional environments in shaping both gut microbiota and brain development (Cerdó et al., 2017; Carlson et al., 2018). These findings are consistent with broader pediatric and public health literature emphasizing early nutrition as a modifiable determinant of long-term cognitive health.

The mechanistic synthesis further suggests that **immune modulation, microbial metabolites, and stress-axis regulation** represent converging biological pathways through which gut dysbiosis may influence neurodevelopment. The predominance of immune and inflammatory pathways across studies aligns with evidence that early immune dysregulation can interfere with synaptic pruning and neural circuit refinement (Arrieta et al., 2014; Sharon et al., 2016). Similarly, the recurring emphasis on short-chain fatty acids highlights the importance of microbial metabolic output as a mediator of brain development, moving the field beyond purely taxonomic descriptions of the microbiome (Cryan et al., 2019; Mayer et al., 2014).

The role of the **hypothalamic–pituitary–adrenal (HPA) axis** deserves particular attention. Early microbial colonization has been shown to shape stress responsivity, and altered stress regulation may act as an intermediary phenotype linking dysbiosis with cognitive and behavioral outcomes (Sudo et al., 2004; O'Mahony et al., 2017). This pathway offers a plausible explanation for why associations are often detected in behavioral and emotional regulation domains, even when direct measures of cognitive performance yield mixed results.

Despite these converging findings, the reviewed literature also reveals substantial **heterogeneity and methodological limitations**. Differences in microbiome assessment techniques, timing of sample collection, neurodevelopmental outcome measures, and population characteristics complicate direct comparisons across studies. Language development, executive function, and social interaction outcomes, in particular, exhibit greater variability, likely reflecting both biological complexity and challenges in measurement during early childhood. These inconsistencies underscore the need for standardized methodologies and longitudinal designs capable of capturing developmental trajectories rather than cross-sectional snapshots (Tamana et al., 2021; Vuong et al., 2017).

From a global pediatric health perspective, the relevance of these findings is amplified in regions characterized by socioeconomic and healthcare disparities. In countries such as Mexico, Colombia, and Ecuador, early-life exposures that influence gut microbiota—such as infection burden, nutritional insecurity, and variable access to healthcare—are particularly prevalent. While much of the existing evidence derives from high-income settings, the biological mechanisms identified in this review are likely to operate across diverse contexts, highlighting the importance of regionally inclusive research and culturally informed preventive strategies (Robertson et al., 2019).

This discussion also emphasizes that **current evidence supports association rather than definitive causation**. While experimental models provide strong mechanistic support, translating these findings into causal inferences in human pediatric populations remains challenging due to ethical, logistical, and methodological constraints. As such, gut dysbiosis should be conceptualized as a contributing factor within a multifactorial developmental framework, interacting with genetics, environment, and psychosocial influences.

CONCLUSIÓN

This review synthesizes current evidence indicating that **early-life gut dysbiosis is closely associated with neurocognitive development in children**, particularly when microbial disruption occurs during sensitive developmental windows. The convergence of findings across experimental models and pediatric human studies supports the concept that the gut microbiota constitutes a key biological interface between early environmental exposures and brain development.

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review

The results highlight that associations between gut dysbiosis and neurodevelopment are most consistently observed in broad cognitive and behavioral domains, with stress reactivity emerging as a recurrent intermediary phenotype. These patterns are biologically plausible given the temporal overlap between microbiome maturation and heightened neurodevelopmental plasticity during infancy and early childhood. Immune modulation, microbial metabolite signaling, and neuroendocrine regulation appear to represent central mechanisms through which early microbial alterations may influence neurocognitive trajectories.

Importantly, this review underscores that early-life gut dysbiosis does not arise in isolation but is shaped by a constellation of clinical, nutritional, and environmental factors, including antibiotic exposure, feeding practices, prematurity, and broader social determinants of health. These findings reinforce the need to view pediatric neurodevelopment within an integrative framework that accounts for both biological systems and contextual influences.

While current evidence predominantly supports associative relationships rather than definitive causality, the consistency of mechanistic pathways and developmental timing across studies strengthens the argument for a meaningful role of the gut microbiota in shaping early brain development. At the same time, heterogeneity in study designs, outcome measures, and microbiome assessment methods highlights important limitations and emphasizes the need for standardized, longitudinal research approaches.

From a pediatric and public health perspective, the findings of this review carry significant implications. Understanding the role of early-life gut dysbiosis may inform preventive strategies aimed at optimizing neurodevelopment through judicious antibiotic use, support for breastfeeding and early nutrition, and microbiome-sensitive care in vulnerable populations. These considerations are particularly relevant in diverse global contexts, including Latin America, where early-life exposures and healthcare inequities may amplify microbiome-related risks.

In conclusion, early-life gut dysbiosis emerges as a biologically grounded and clinically relevant factor in pediatric neurocognitive development. Continued interdisciplinary research integrating microbiology, neuroscience, pediatrics, and public health is essential to clarify causal pathways and translate microbiome science into evidence-based strategies that support optimal developmental outcomes in children.

REFERENCIAS

1. Arrieta, M. C., Stiemsma, L. T., Amenyogbe, N., Brown, E. M., & Finlay, B. (2014). The intestinal microbiome in early life. *Frontiers in Immunology, 5*, 427. https://doi.org/10.3389/fimmu.2014.00427
2. Berding, K., & Donovan, S. M. (2016). Microbiome and nutrition in autism spectrum disorder. *Current Opinion in Clinical Nutrition & Metabolic Care, 19*(3), 205–210. https://doi.org/10.1097/MCO.0000000000000279
3. Borre, Y. E., O'Keeffe, G. W., Clarke, G., Stanton, C., Dinan, T. G., & Cryan, J. F. (2014). Microbiota and neurodevelopmental windows: Implications for brain disorders. *Trends in Molecular Medicine, 20*(9), 509–518. https://doi.org/10.1016/j.molmed.2014.05.002
4. Carlson, A. L., Xia, K., Azcarate-Peril, M. A., Goldman, B. D., Ahn, M., Styner, M. A., … Knickmeyer, R. C. (2018). Infant gut microbiome associated with cognitive development. *Biological Psychiatry, 83*(2), 148–159. https://doi.org/10.1016/j.biopsych.2017.06.021
5. Cerdó, T., Ruíz, A., Suárez, A., & Campoy, C. (2017). Probiotic, prebiotic, and brain development. *Nutrients, 9*(11), 1247. https://doi.org/10.3390/nu9111247
6. Cong, X., Xu, W., Romisher, R., Poveda, S., Forte, S., Starkweather, A., & Henderson, W. A. (2016). Gut microbiome and neurodevelopment in preterm infants. *Biological Research for Nursing, 18*(4), 431–438. https://doi.org/10.1177/1099800416629593
7. Cryan, J. F., O'Riordan, K. J., Cowan, C. S. M., Sandhu, K. V., Bastiaanssen, T. F. S., Boehme, M., … Dinan, T. G. (2019). The microbiota–gut–brain axis. *Physiological Reviews, 99*(4), 1877–2013. https://doi.org/10.1152/physrev.00018.2018
8. Diaz Heijtz, R., Wang, S., Anuar, F., Qian, Y., Björkholm, B., Samuelsson, A., … Pettersson, S. (2011). Normal gut microbiota modulates brain development and behavior. *Proceedings of the National Academy of Sciences, 108*(7), 3047–3052. https://doi.org/10.1073/pnas.1010529108
9. Dinan, T. G., & Cryan, J. F. (2017). Gut instincts: Microbiota as a key regulator of brain development. *Trends in Neurosciences, 40*(9), 558–570. https://doi.org/10.1016/j.tins.2017.06.001

10. Hsiao, E. Y., McBride, S. W., Hsien, S., Sharon, G., Hyde, E. R., McCue, T., … Mazmanian, S. K. (2013). Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell, 155*(7), 1451–1463. https://doi.org/10.1016/j.cell.2013.11.024
11. Johnson, C. L., & Versalovic, J. (2012). The human microbiome and its potential importance to pediatrics. *Pediatrics, 129*(5), 950–960. https://doi.org/10.1542/peds.2011-2736
12. Mayer, E. A., Knight, R., Mazmanian, S. K., Cryan, J. F., & Tillisch, K. (2014). Gut microbes and the brain: Paradigm shift in neuroscience. *The Journal of Neuroscience, 34*(46), 15490–15496. https://doi.org/10.1523/JNEUROSCI.3299-14.2014
13. O'Mahony, S. M., Clarke, G., Dinan, T. G., & Cryan, J. F. (2017). Early-life adversity and brain development: Is the microbiome a missing piece? *Neuroscience, 342*, 37–54. https://doi.org/10.1016/j.neuroscience.2015.09.068
14. Ridaura, V. K., Faith, J. J., Rey, F. E., Cheng, J., Duncan, A. E., Kau, A. L., … Gordon, J. I. (2013). Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science, 341*(6150), 1241214. https://doi.org/10.1126/science.1241214
15. Robertson, R. C., Manges, A. R., Finlay, B. B., & Prendergast, A. J. (2019). The human microbiome and child growth. *Pediatrics, 143*(6), e20190136. https://doi.org/10.1542/peds.2019-0136
16. Sharon, G., Sampson, T. R., Geschwind, D. H., & Mazmanian, S. K. (2016). The central nervous system and the gut microbiome. *Cell, 167*(4), 915–932. https://doi.org/10.1016/j.cell.2016.10.027
17. Slykerman, R. F., Thompson, J., Waldie, K. E., Murphy, R., Wall, C., & Mitchell, E. A. (2017). Antibiotics in the first year of life and subsequent neurocognitive outcomes. *Acta Paediatrica, 106*(1), 87–94. https://doi.org/10.1111/apa.13613
18. Sudo, N., Chida, Y., Aiba, Y., Sonoda, J., Oyama, N., Yu, X. N., … Koga, Y. (2004). Postnatal microbial colonization programs the hypothalamic–pituitary–adrenal system. *The Journal of Physiology, 558*(1), 263–275. https://doi.org/10.1113/jphysiol.2004.063388
19. Tamana, S. K., Tun, H. M., Konya, T., Chari, R. S., Field, C. J., Guttman, D. S., … Azad, M. B. (2021). Gut microbiota composition and cognitive development in early childhood. *EClinicalMedicine, 31*, 100705. https://doi.org/10.1016/j.eclinm.2020.100705
20. Vuong, H. E., Yano, J. M., Fung, T. C., & Hsiao, E. Y. (2017). The microbiome–gut–brain axis during early life. *Nature Reviews Gastroenterology & Hepatology, 14*(10), 623–635. https://doi.org/10.1038/nrgastro.2017.58

Edición 3, Año 2, Número 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 3, Year 2, Number 2, 2025
E-ISSN: 3061-8045, P-ISSN: 3061-8517
IECCMEXICO Review