International Journal of Science, Strategic Management and Technology
Volume **02** Issue **03** March-**2026** | ISSN: **3108-1762 (Online)** | Impact Factor: 3.8
An International, Peer-Reviewed, Open Access Scholarly Journal Indexed in recognized academic databases

Targeting the Gut–Brain–Immune Axis: Emerging Pharmacological Strategies for Neuroinflammatory Disorders

Mr. Utkarsh R. Mandage, Mr. Prasad P. Duphare, Ms. Prajakta S. Mahajan.

1. Lecturer, Departmeent of Pharmacognosy, Ravindra Vidya Prasarak Mandal Institute of Pharmacy, Dwarka, Nashik, Maharashtra, India.
2. Lecturer, Department of Pharmaceutics, Ashoka Institute of Pharmacy, Chandrapur, Maharashtra, India.
3. Assistant Professor, Department of Pharmacology, Shram Sadhana Bombey Trust Institute of Pharmacy, Bambhori, Jalgaon, Maharashtra, India

https://doi.org/10.55041/ijsmt.v2i3.268

Cite this Article: Mandage, U. R. & Duphare, P. P. (2026). Targeting the Gut–Brain–Immune Axis: Emerging Pharmacological Strategies for Neuroinflammatory Disorders. International Journal of Science, Strategic Management and Technology, *02*(03). https://doi.org/10.55041/ijsmt.v2i3.268

1. Graphical Abstract:

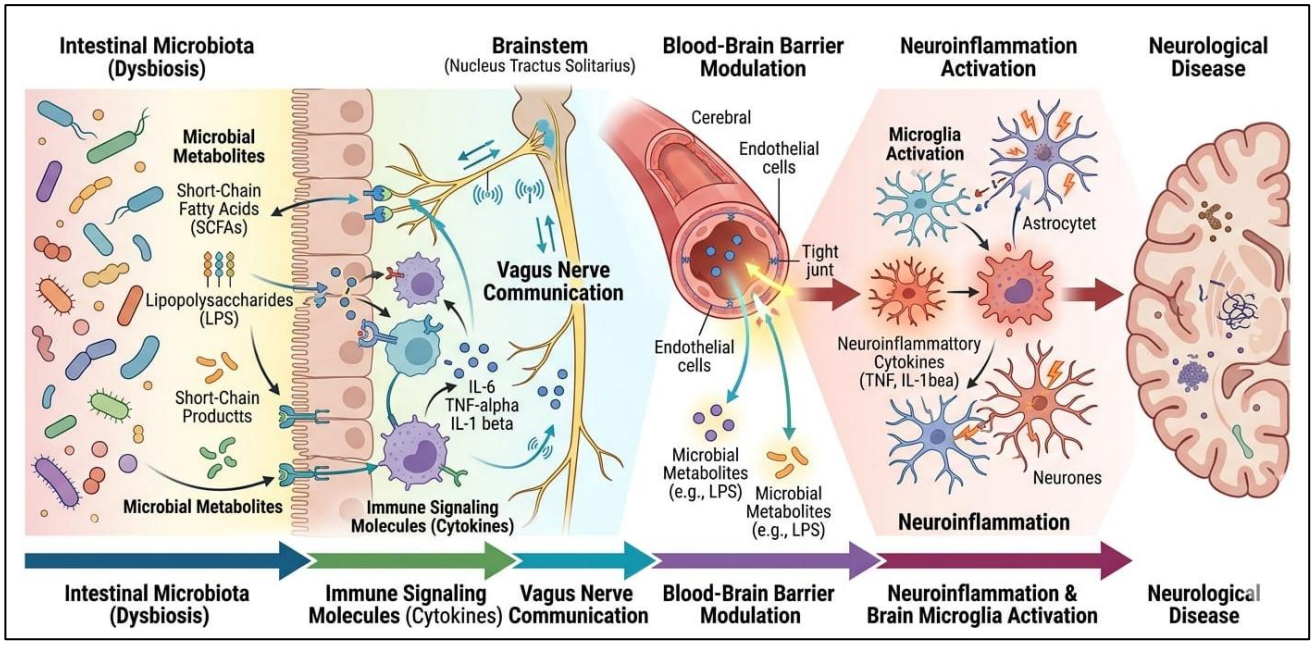

Figure 1: Pathophysiological mechanisms of the gut–microbiota–brain axis in neuroinflammation.

2. Abstract:

Neuroinflammation plays a central role in the development and progression of several neurological and neurodegenerative disorders. In recent years, increasing scientific evidence has demonstrated that the gut microbiota interacts closely with the immune system and the central nervous system (CNS) through a complex communication network known as the gut–brain–immune axis. This bidirectional system integrates neural, endocrine, metabolic, and immune signaling pathways that regulate brain function and systemic immune responses. Disturbances in gut microbial composition, commonly referred to as gut dysbiosis, have been linked to increased intestinal permeability, systemic inflammation, and activation of neuroinflammatory pathways. The present review aims to explore the structural and functional components of the gut–brain–immune axis and to summarize the molecular mechanisms through which gut microbiota influences neuroinflammatory processes and neurological disorders. A comprehensive literature review was conducted using major scientific databases including PubMed, Scopus, and Google Scholar. Relevant peer-reviewed articles, reviews, and experimental studies published in recent years were selected using keywords related to gut microbiota, neuroinflammation, immune signaling, and microbiome-based therapies. The selected studies were critically analyzed to identify key mechanisms and therapeutic developments. The findings suggest that gut microbiota significantly influences neuroinflammatory responses through multiple mechanisms, including microbial metabolite production, cytokine-mediated immune signaling, neuroendocrine pathways, and vagus nerve communication. Dysregulation of this axis has been associated with neurological conditions such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, autism spectrum disorder, and major depressive disorder. Recent pharmacological research has focused on microbiome-targeted interventions such as probiotics, prebiotics, synbiotics, dietary modulation, and fecal microbiota transplantation. Additionally, natural compounds including curcumin, polyphenols, and adaptogenic herbs have shown potential neuroprotective and anti-inflammatory effects through modulation of gut microbial balance. Understanding the interactions between gut microbiota, immune signaling pathways, and neural mechanisms may provide novel therapeutic strategies for managing neuroinflammatory diseases. Targeting the gut–brain–immune axis therefore represents a promising direction for future pharmacological research and the development of innovative treatments.

Keywords: Gut microbiota; neuroinflammation; immune signaling; microbiome therapeutics; pharmacological targets; neurodegenerative diseases; gut–brain axis

3. Introduction:

3.1. Overview of Neuroinflammation in Neurological Disorders-

Neuroinflammation has emerged as a key biological process involved in the development and progression of many neurological and neurodegenerative disorders. It refers to the inflammatory response that occurs within the central nervous system (CNS), primarily mediated by immune cells such as microglia and astrocytes. While acute neuroinflammatory responses may play a protective role in maintaining neural homeostasis and defending against pathogens, chronic or uncontrolled inflammation can lead to neuronal damage and impaired brain function. Persistent activation of inflammatory pathways has been associated with progressive neuronal degeneration and disruption of normal neural signaling [4, 17, 29].

A growing body of evidence indicates that neuroinflammation contributes significantly to the pathology of several major neurological disorders. These include Alzheimer's disease, Parkinson's disease, Multiple sclerosis, Autism spectrum disorder, and Major depressive disorder. In these conditions, inflammatory mediators such as cytokines, chemokines, and reactive oxygen species contribute to neuronal injury, synaptic dysfunction, and progressive neurodegeneration [6, 9, 24]. Understanding the underlying mechanisms that regulate neuroinflammatory responses has therefore become a critical area of research in neuroscience and pharmacology.

3.2. Importance of Gut Microbiota in Human Health-

The human gastrointestinal tract contains a highly complex community of microorganisms collectively known as the Gut microbiota. This microbial ecosystem consists of bacteria, fungi, viruses, and other microorganisms that coexist with the host and perform numerous essential physiological functions. These microbes contribute to digestion, synthesis of vitamins, regulation of metabolism, and maintenance of immune system balance [18, 28]. In recent years, scientific studies have revealed that gut microbiota also plays a significant role in influencing brain function and behavior [8, 21].

A healthy microbial balance is essential for maintaining intestinal integrity and immune homeostasis. However, disturbances in microbial composition, often referred to as dysbiosis, can disrupt intestinal barrier function and promote systemic inflammation. Dysbiosis has been associated with metabolic disorders, immune dysfunction, and several neurological conditions [24, 31]. Because of this strong connection between gut microbes and systemic physiology, the gut microbiota is increasingly recognized as a critical factor in overall human health.

3.3. Concept and Evolution of the Gut–Brain–Immune Axis-

The relationship between the gastrointestinal system and the brain has been described through the concept of the Gut–brain axis, which represents a bidirectional communication network linking the central nervous system with the gastrointestinal tract. More recently, researchers have expanded this concept to include the immune system, leading to the broader framework known as the Gut–brain–immune axis [1, 3, 33]. This integrated system involves neural, hormonal, metabolic, and immune signaling pathways that allow continuous communication between the gut microbiota and the brain. Communication along this axis occurs through several mechanisms, including microbial metabolite production, immune signaling molecules, neuroendocrine pathways, and direct neural communication via the Vagus nerve. Microbial metabolites such as short-chain fatty acids can influence immune responses and modulate neural activity [11, 34]. Similarly, cytokines produced during immune activation can affect brain function and behavior. These interactions demonstrate that the gut microbiota plays an active role in regulating neuroinflammatory processes and neurological health.

3.4. Rationale for Targeting the Gut–Brain–Immune Axis in Pharmacological Therapy-

Increasing scientific evidence has highlighted the complex interactions between the Gut microbiota, immune signaling pathways, and neural communication systems. These interactions collectively form the Gut–brain–immune axis, which plays a crucial role in maintaining neurological and immunological homeostasis. Disruption of this regulatory network has been associated with chronic inflammation, neurodegeneration, and alterations in cognitive and emotional functions [9, 39]. Because of its central role in regulating immune responses and neural signaling, the gut–brain–immune axis has emerged as a promising target in modern pharmacological and biomedical research. Dysbiosis of gut microbial communities may lead to increased intestinal permeability, systemic immune activation, and the release of pro-inflammatory mediators that contribute to neuroinflammatory processes.

Recent therapeutic strategies aim to restore microbial balance and regulate immune responses through microbiome-based interventions. Approaches such as Probiotics, Prebiotics, dietary modulation, and microbiota-targeted therapies have demonstrated potential in reducing inflammatory signaling and improving neurological health [15, 36]. In addition, several natural bioactive compounds and plant-derived phytochemicals are being investigated for their ability to modulate gut microbial composition and exert neuroprotective and anti-inflammatory effects. Targeting the gut–brain–immune axis therefore represents an innovative therapeutic strategy for preventing and managing neuroinflammatory and neurodegenerative disorders.

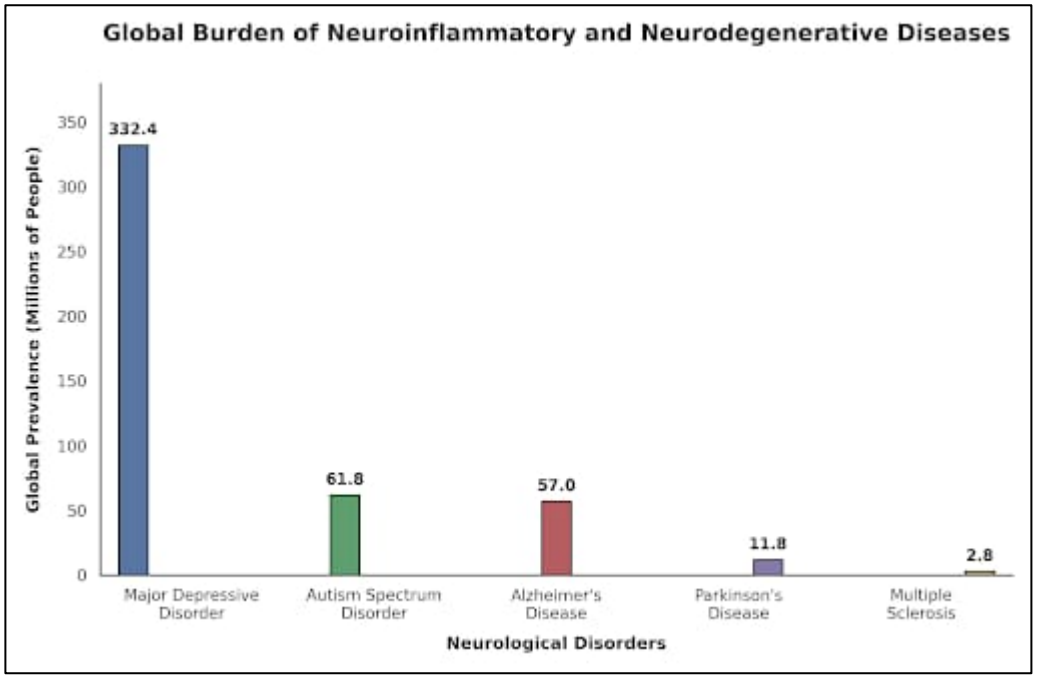

Figure 2: Graphical representation of the global burden of neuroinflammatory and neurodegenerative diseases.

This bar graph illustrates the global burden of major neuroinflammatory and neurodegenerative diseases. The data is based on the most recent estimates from the Global Burden of Disease (GBD) 2021 study and World Health Organization (WHO) reports.

Key Insights from the Data:

- Major Depressive Disorder (MDD): Affects approximately 332.4 million people, representing the highest burden among the conditions listed. It is a leading cause of non-fatal health loss globally.
- Autism Spectrum Disorder (ASD): Recent GBD 2021 estimates indicate a global prevalence of 61.8 million, reflecting improved diagnostic screening and awareness.
- Alzheimer's Disease & Dementias: Approximately 57.0 million people live with dementia worldwide, with Alzheimer's disease accounting for 60–80% of these cases. This number is projected to triple by 2050.
- Parkinson's Disease (PD): Affects roughly 11.8 million individuals. It is currently the fastest-growing neurological disorder in terms of prevalence, disability, and deaths.
- Multiple Sclerosis (MS): Affects approximately 2.8 million people. While it has the lowest total prevalence on this list, it primarily impacts young adults and carries a significant long-term disability burden.

4. Structural Components of the Gut–Brain–Immune Axis:

The Gut–brain–immune axis represents an integrated biological network that connects the gastrointestinal tract, immune system, and central nervous system. This system enables continuous communication between the gut environment and the brain through neural, endocrine, metabolic, and immune pathways. Several structural and functional components contribute to this complex interaction, including the gut microbiota, intestinal barrier, immune cells, neural networks of the gut, and the integrity of the blood–brain barrier [1, 3, 4]. Together, these components regulate immune responses, maintain intestinal homeostasis, and influence neurological function.

4.1. Gut Microbiota Composition-

The Gut microbiota refers to the diverse community of microorganisms residing in the gastrointestinal tract. It is estimated that trillions of microbes inhabit the human intestine, consisting mainly of bacteria belonging to the phyla Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria [18, 31]. These microbial communities perform several essential physiological functions, including digestion of dietary components, production of vitamins, and regulation of host metabolism. In addition to metabolic roles, gut microbiota significantly influences immune system development and function. Microbial metabolites such as short-chain fatty acids (SCFAs) can regulate inflammatory pathways and modulate immune cell activity [11, 28]. However, disruption of microbial balance, commonly known as dysbiosis, can lead to increased intestinal permeability and systemic inflammation, which may contribute to neuroinflammatory and neurodegenerative disorders [9, 24].

4.2. Intestinal Epithelial Barrier-

The Intestinal epithelial barrier forms the primary physical and functional barrier between the intestinal lumen and the internal environment of the body. It is composed of a single layer of epithelial cells connected by tight junction proteins that regulate the selective permeability of molecules. This barrier plays a crucial role in preventing the entry of harmful pathogens, toxins, and antigens into the systemic circulation [12, 28].

A healthy intestinal barrier also supports communication between gut microbes and host immune cells. When the integrity of this barrier is compromised, a condition often referred to as “leaky gut,” microbial products and inflammatory mediators may enter the bloodstream. This can trigger systemic immune responses and contribute to neuroinflammatory processes within the central nervous system [12, 14].

4.3. Immune Cell Populations in the Gut-

The gastrointestinal tract contains one of the largest immune compartments in the human body, known as the Gut-associated lymphoid tissue (GALT). This immune system includes various immune cell populations such as macrophages, dendritic cells, T lymphocytes, B lymphocytes, and innate lymphoid cells [28, 38]. These immune cells constantly interact with gut microbiota to maintain immune tolerance while defending the body against harmful pathogens. Cytokines and chemokines released by these immune cells can influence systemic inflammation and communicate signals to the brain. Dysregulation of immune responses within the gut may therefore contribute to chronic inflammation and neurological disorders [4, 17].

4.4. Neural Communication (Enteric Nervous System)-

Neural communication between the gut and brain is primarily mediated by the Enteric nervous system, which is often referred to as the “second brain.” This complex network of neurons embedded within the gastrointestinal tract regulates digestive functions such as motility, secretion, and blood flow [8, 21].

Signals from the enteric nervous system are transmitted to the central nervous system through neural pathways including the Vagus nerve [10, 19]. Microbial metabolites and immune mediators can influence neuronal signaling, thereby affecting brain function, mood, and cognitive processes. This neural communication represents an important pathway through which gut microbiota can impact neurological health.

International Journal of Science, Strategic Management and Technology
Volume **02** Issue **03** March-**2026** | ISSN: **3108-1762 (Online)** | Impact Factor: 3.8
An International, Peer-Reviewed, Open Access Scholarly Journal Indexed in recognized academic databases

4.5. Blood–Brain Barrier Integrity-

The Blood–brain barrier is a highly selective protective barrier that separates the circulating blood from brain tissue. It is composed of endothelial cells connected by tight junctions, supported by astrocytes and pericytes. This barrier plays a critical role in maintaining the stable microenvironment required for proper neuronal function [12, 14].

Inflammatory mediators and microbial metabolites generated in the gut can influence the permeability of the blood–brain barrier. Disruption of this barrier may allow harmful substances and immune cells to enter the brain, leading to neuroinflammation and neuronal damage [14, 29]. Therefore, maintaining the integrity of the blood–brain barrier is essential for protecting the central nervous system from systemic inflammatory signals originating in the gut.

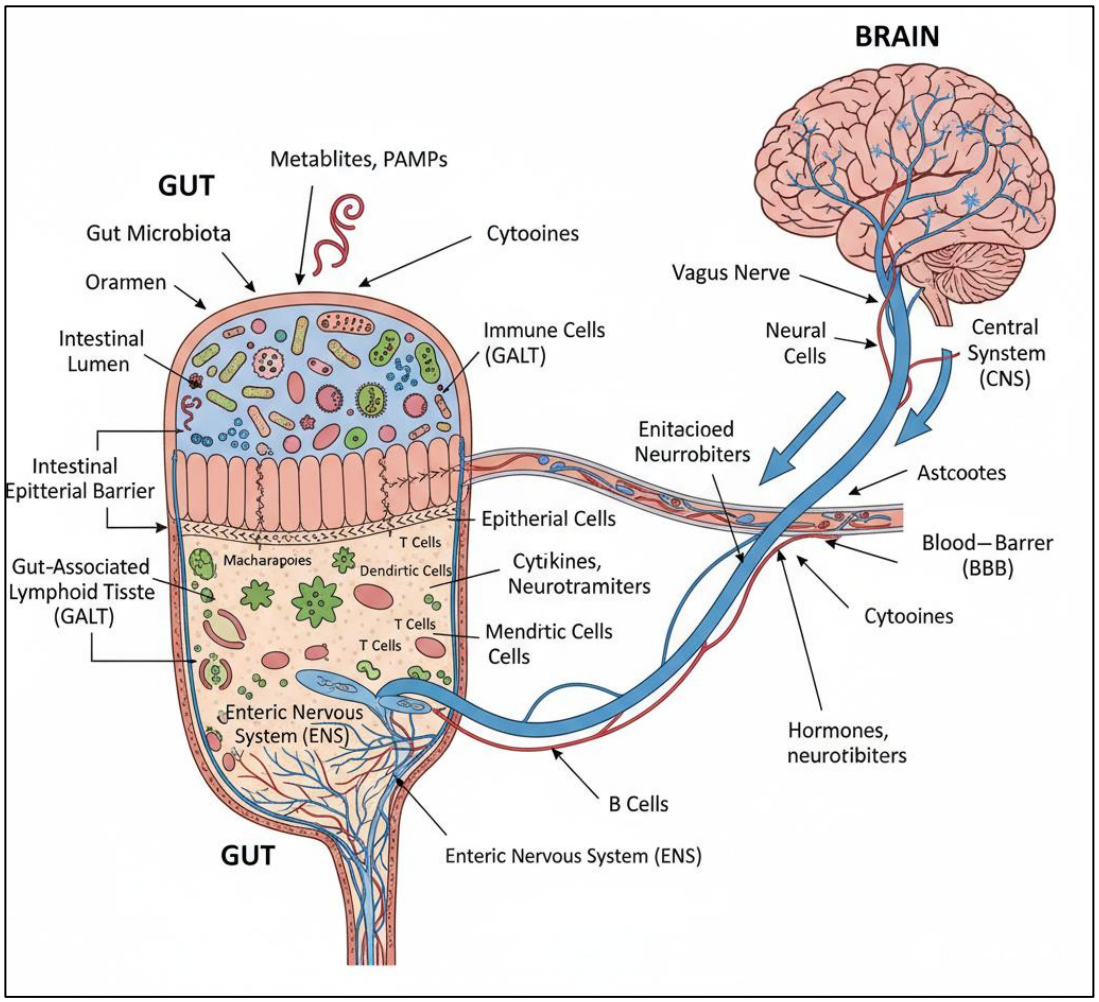

Figure 3: Structural components of the gut–brain–immune axis.

(A schematic diagram illustrating the major components of the gut–brain–immune axis, including gut microbiota, intestinal epithelial barrier, immune cell populations, enteric nervous system communication, vagus nerve signaling, and the blood–brain barrier.)

5. Molecular Mechanisms Linking Gut Microbiota and Neuroinflammation:

The interaction between the Gut microbiota and the central nervous system plays an essential role in regulating immune balance and neural health. Increasing scientific evidence indicates that alterations in gut microbial composition can influence inflammatory processes in the brain through several molecular pathways. These pathways involve microbial

metabolites, immune mediators, neuroendocrine signaling, and neural communication networks. Together, these mechanisms form the functional basis of the Gut–brain–immune axis, enabling bidirectional communication between the gut and the brain [1, 4, 9].

5.1. Microbial Metabolite Signaling-

One of the most important mechanisms linking gut microbiota to brain function involves the production of bioactive microbial metabolites. These metabolites are generated when intestinal microorganisms metabolize dietary components such as fiber, amino acids, and bile salts. Many of these compounds can enter systemic circulation and influence immune responses, neuronal activity, and brain physiology [31, 34].

Among these metabolites, Short-chain fatty acids (SCFAs) are particularly important. SCFAs, including acetate, propionate, and butyrate, are produced during the fermentation of dietary fiber by gut bacteria. These molecules help regulate inflammatory pathways, strengthen intestinal barrier integrity, and support immune system balance [11, 31]. Butyrate, in particular, has been shown to possess anti-inflammatory properties and may contribute to the protection of neuronal cells. Another group of important compounds includes Tryptophan metabolites, which are derived from the microbial metabolism of the amino acid tryptophan. These metabolites influence neurotransmitter synthesis and immune signaling pathways, thereby affecting mood regulation, cognitive function, and neuroinflammatory responses [31, 32]. In addition, microbial modification of Bile acids generates secondary bile acids that can act as signaling molecules influencing immune and metabolic pathways [31]. Through these metabolite-mediated interactions, gut microbiota can exert a significant influence on brain health and inflammation.

5.2. Cytokine-Mediated Immune Response-

Gut microbiota also influences neuroinflammation through modulation of immune signaling pathways. The intestinal immune system constantly interacts with microbial communities to maintain immune tolerance and defense against pathogens. When microbial balance is disturbed, immune cells may release pro-inflammatory mediators that can affect distant organs, including the brain [28, 38].

Cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β) are key regulators of inflammatory responses. Elevated levels of these cytokines may promote systemic inflammation and contribute to activation of immune cells within the central nervous system [4, 17]. Once these inflammatory signals reach the brain, they can stimulate microglial activation and trigger neuroinflammatory cascades. Persistent cytokine-mediated signaling is therefore considered a critical link between gut dysbiosis and neurological disorders [29].

5.3. Neuroendocrine Signaling-

Another important pathway connecting gut microbiota to brain function involves neuroendocrine signaling. The gut microbiota can influence hormonal pathways associated with stress and metabolic regulation. One of the major systems involved in this process is the Hypothalamic–pituitary–adrenal axis, which controls the body's response to stress [13, 40].

Alterations in gut microbial composition can modify the activity of this axis and affect the production of stress hormones such as cortisol. Increased cortisol levels may promote inflammatory responses and disrupt normal neuronal signaling. Through interactions with endocrine pathways, gut microbes therefore contribute to the regulation of stress responses and neuroinflammatory processes [13, 40].

International Journal of Science, Strategic Management and Technology
Volume **02** Issue **03** March-**2026** | ISSN: **3108-1762 (Online)** | Impact Factor: 3.8
An International, Peer-Reviewed, Open Access Scholarly Journal Indexed in recognized academic databases

5.4. Vagus Nerve Activation-

Direct neural communication between the gut and brain is primarily mediated through the Vagus nerve, which forms a major component of the gut–brain signaling pathway [10, 19]. Sensory neurons in the gastrointestinal tract can detect microbial metabolites, immune mediators, and chemical signals generated by gut microorganisms.

Activation of vagal pathways allows rapid transmission of signals from the gut to the brain. These signals can influence neurotransmitter release, inflammatory responses, and behavioral processes. Experimental studies have demonstrated that modulation of vagus nerve activity can significantly alter immune responses and reduce neuroinflammation [10, 33]. Therefore, vagus nerve signaling represents a crucial neural mechanism linking gut microbial activity with brain function.

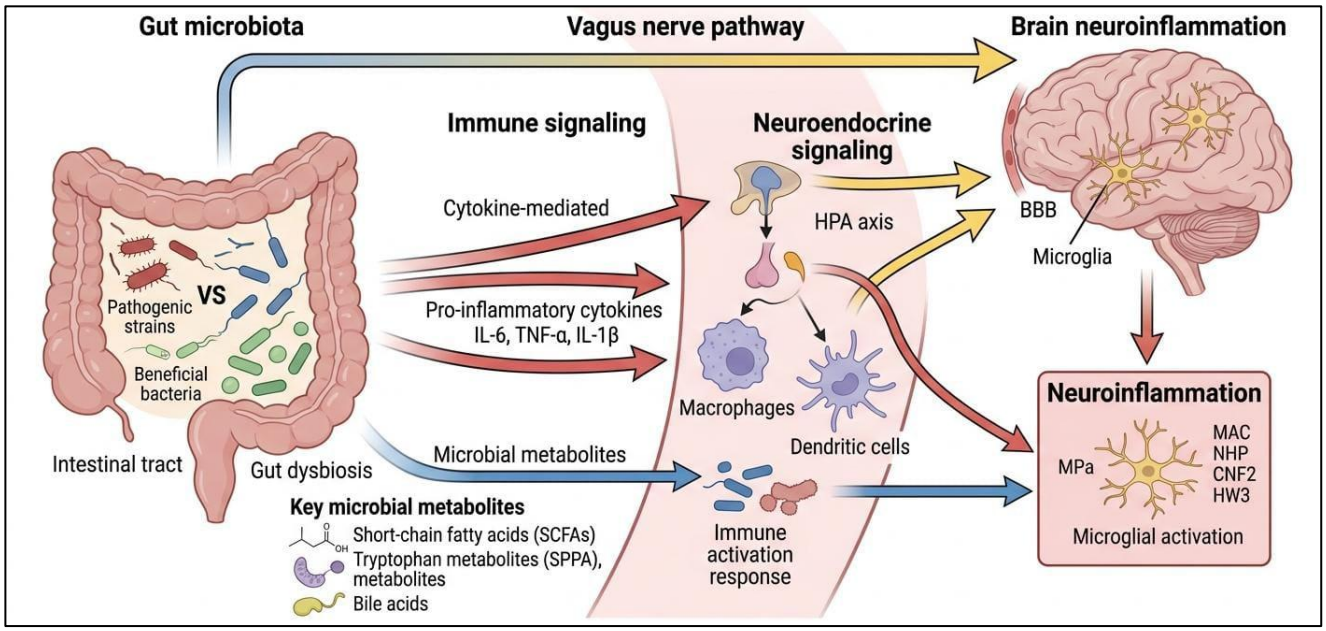

Figure 4: Molecular pathways connecting gut dysbiosis to brain inflammation.

(A schematic illustration demonstrating how alterations in gut microbiota lead to the production of microbial metabolites, activation of immune cytokines, stimulation of neuroendocrine pathways, and vagus nerve signaling, ultimately contributing to neuroinflammatory processes in the brain.)

6. Role of Gut Dysbiosis in Neuroinflammatory Disorders:

Disturbances in the normal composition and function of the Gut microbiota are commonly referred to as Gut dysbiosis. This imbalance may occur due to several factors such as poor diet, antibiotic overuse, infections, environmental stress, and lifestyle changes. Increasing scientific evidence suggests that gut dysbiosis plays a significant role in the development and progression of neuroinflammatory and neurodegenerative disorders. Altered microbial communities can influence immune responses, metabolic signaling, and neural communication, thereby contributing to disease pathogenesis [9, 24, 31].

One important mechanism through which dysbiosis contributes to neurological disorders is the production of microbial toxins and harmful metabolites. Certain pathogenic bacteria may release endotoxins such as lipopolysaccharides that stimulate inflammatory responses within the body. These microbial toxins can cross the intestinal barrier and enter systemic circulation, triggering immune activation and inflammatory signaling pathways. Chronic exposure to these inflammatory mediators may ultimately affect brain function and contribute to neurodegenerative processes [28, 38]. Another critical factor linking gut dysbiosis to neurological disease is the activation of inflammatory signaling cascades. Imbalanced microbial populations may stimulate immune cells within the intestinal environment, leading to increased

production of pro-inflammatory cytokines. These cytokines can circulate through the bloodstream and influence inflammatory responses in the central nervous system. Persistent inflammatory signaling can promote neuronal damage and disrupt normal neural communication [4, 17].

Gut dysbiosis is also associated with activation of Microglia, the resident immune cells of the brain. Under normal conditions, microglia help maintain neural homeostasis and protect the brain from infections. However, excessive or prolonged activation of microglia can lead to the release of inflammatory mediators, reactive oxygen species, and neurotoxic substances. This process contributes to neuronal injury and plays a central role in the progression of many neuroinflammatory disorders [29]. Several neurological diseases have been associated with distinct alterations in gut microbial composition. For example, Alzheimer's disease has been linked to a reduction in beneficial bacteria that normally produce anti-inflammatory metabolites [26]. In Parkinson's disease, increased levels of pro-inflammatory microbial species may promote inflammation and contribute to the degeneration of dopaminergic neurons [25, 30]. Similarly, Multiple sclerosis has been associated with microbial changes that influence immune regulation and promote autoimmune responses against the myelin sheath of neurons [27].

These findings highlight the importance of maintaining a balanced gut microbial ecosystem for neurological health. Understanding the relationship between gut dysbiosis and neuroinflammation may help identify new therapeutic strategies aimed at restoring microbial balance and reducing disease progression [39].

Table 1. Alterations in Gut Microbiota Associated with Neurological Diseases

Disease	**Microbial Change**	**Pathological Effect**
Alzheimer's disease	Reduced beneficial bacteria	Increased neuroinflammation and neuronal damage
Parkinson's disease	Increased inflammatory microbial species	Degeneration of dopaminergic neurons
Multiple sclerosis	Microbial imbalance leading to immune dysregulation	Demyelination and autoimmune inflammation

7. Immune Pathways in the Gut–Brain Axis-

The Gut–brain axis is strongly influenced by immune signaling pathways that connect intestinal immune responses with inflammatory processes in the central nervous system. The immune system serves as a key mediator in communication between gut microbiota and the brain. When microbial balance in the gut is disrupted, immune pathways can become activated, leading to the release of inflammatory mediators that may affect neural tissues. These immune responses involve cytokine signaling networks, activation of glial cells, receptor-mediated inflammatory pathways, and immune cell migration [4, 17, 28]. Understanding these immune mechanisms is essential for explaining how intestinal inflammation contributes to neuroinflammatory disorders and neurological damage.

7.1. Cytokine Signaling Networks-

Cytokines are small signaling proteins that regulate immune responses and inflammation. In the gut–brain axis, cytokines produced within the intestinal environment can enter systemic circulation and influence immune activity in the brain. Increased levels of pro-inflammatory cytokines are often associated with chronic inflammation and neuronal damage [4, 17].

Key inflammatory mediators include Interleukin-6 (IL-6), Tumor necrosis factor-alpha (TNF-α), and Interleukin-1 beta (IL-1β). These cytokines can promote inflammatory signaling cascades that activate immune cells in the central nervous system. Elevated cytokine levels have been linked to several neurodegenerative disorders and may contribute to neuronal dysfunction and cognitive impairment [17, 29].

7.2. Activation of Microglia and Astrocytes-

Immune signaling from the gut can influence the activity of glial cells in the brain, particularly Microglia and Astrocytes. Microglia are the primary immune cells of the central nervous system and play an important role in maintaining neural homeostasis and defending against pathogens. Astrocytes support neuronal metabolism, regulate neurotransmitter balance, and contribute to blood–brain barrier stability [29, 37].

When exposed to inflammatory signals originating from gut dysbiosis, these glial cells may become excessively activated. Activated microglia release inflammatory mediators, reactive oxygen species, and neurotoxic substances that can damage neurons. Similarly, activated astrocytes may amplify inflammatory signaling within brain tissues. Persistent glial activation therefore contributes to the development and progression of neuroinflammatory disorders [29].

7.3. Toll-Like Receptor–Mediated Inflammation-

Another important immune pathway involved in gut–brain communication is mediated through Toll-like receptors (TLRs). These receptors are pattern-recognition molecules expressed on immune cells that detect microbial components such as bacterial lipopolysaccharides and other pathogen-associated molecular patterns [28, 38].

Activation of Toll-like receptors triggers intracellular signaling pathways that lead to the production of pro-inflammatory cytokines and immune mediators. In conditions of gut dysbiosis, excessive microbial components may stimulate TLR signaling, promoting systemic inflammation. This inflammatory response can extend to the brain and contribute to neuroinflammatory damage [28, 38].

7.4. Role of T-Cells and Macrophages-

Adaptive and innate immune cells also play a critical role in linking gut inflammation with neurological processes. T-cells are essential components of adaptive immunity and are responsible for regulating immune responses against pathogens while maintaining immune tolerance. In certain inflammatory conditions, activated T-cells may migrate from peripheral tissues into the central nervous system, where they contribute to inflammatory damage [27].

Similarly, Macrophages are innate immune cells that participate in pathogen clearance and inflammatory regulation. In response to microbial imbalance, macrophages may produce cytokines and chemokines that amplify immune responses. The combined activity of T-cells and macrophages can therefore enhance inflammatory signaling between the gut and brain, contributing to neuroinflammation and neuronal injury [27, 28].

Important Immune Mediators

Several inflammatory mediators play central roles in gut–brain immune signaling:

- Interleukin-6 (IL-6) – promotes inflammatory responses and immune activation
- Tumor necrosis factor-alpha (TNF-α) – a major regulator of systemic inflammation
- Interleukin-1 beta (IL-1β) – contributes to neuronal inflammation and immune signaling

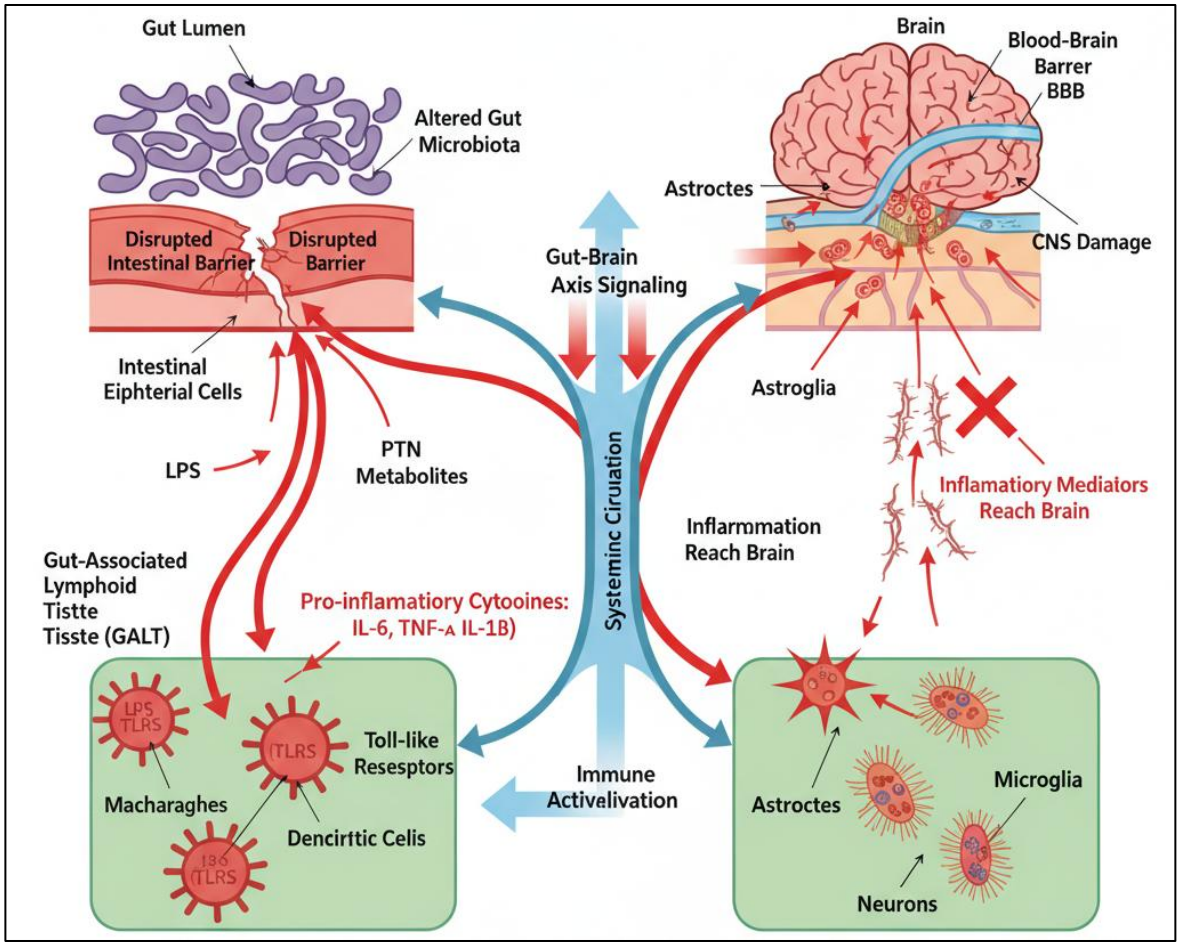

Figure 5: Immune signaling cascade linking gut inflammation to CNS damage.

(A conceptual diagram showing how gut dysbiosis triggers immune activation, leading to cytokine release (IL-6, TNF-α, IL-1β), Toll-like receptor signaling, activation of microglia and astrocytes, and subsequent neuroinflammatory damage within the brain.)

8. Pharmacological Targets within the Gut–Brain–Immune Axis:

Advances in research on the Gut–brain–immune axis have created new possibilities for developing therapeutic approaches aimed at controlling neuroinflammation and neurological disorders. Because this axis involves complex interactions among gut microorganisms, immune pathways, and neural signaling networks, several pharmacological targets have been identified. Targeting these mechanisms may help regulate inflammatory responses, maintain microbial balance, and protect neuronal tissues from damage [4,31,39].

One potential strategy involves the modulation of Microbial enzymes produced by intestinal microorganisms. These enzymes participate in the metabolism of dietary substrates and generate bioactive metabolites that influence immune signaling and brain function. Therapeutic agents or microbiome-modulating interventions that regulate microbial enzymatic activity may help restore metabolic homeostasis and reduce inflammatory signaling within the gut–brain axis [31,34].

Another important pharmacological target includes inflammatory cytokines such as Tumor necrosis factor-alpha, Interleukin-6, and Interleukin-1 beta. These mediators play a central role in immune activation and the progression of neuroinflammatory responses. Therapeutic agents, including Monoclonal antibodies and cytokine inhibitors, are currently

being explored for their ability to suppress excessive inflammatory signaling and reduce neuronal injury associated with chronic inflammation [17,28].

Regulation of Microglia activation represents another promising therapeutic strategy. Microglial cells function as the primary immune components of the central nervous system and are responsible for maintaining neural homeostasis. However, prolonged or excessive activation of these cells can lead to the release of inflammatory mediators and neurotoxic molecules, contributing to neuronal damage. Consequently, Neuroprotective drugs that modulate microglial activity are being investigated as potential treatments for neurodegenerative conditions [29,37].

Neural communication pathways also provide important pharmacological targets within this axis. The Vagus nerve acts as a major signaling pathway connecting the gastrointestinal tract with the brain. Pharmacological modulation or neuromodulatory techniques that influence vagal signaling may help regulate immune responses and improve neurological outcomes by reducing systemic inflammation [10,33].

Another important therapeutic focus is the preservation of Blood–brain barrier integrity. The blood–brain barrier acts as a protective interface that regulates the passage of molecules between the bloodstream and neural tissue. Disruption of this barrier can allow inflammatory mediators and toxins to enter the brain, thereby aggravating neuroinflammation. Therapeutic strategies aimed at strengthening blood–brain barrier function may therefore help prevent inflammatory damage within the central nervous system [37].

Overall, these pharmacological targets represent promising directions for the development of innovative therapies designed to regulate immune signaling, protect neuronal health, and restore balance within the gut–brain–immune axis.

Table 2. Potential Drug Targets in the Gut–Brain–Immune Axis

Target	**Drug Category**	**Therapeutic Potential**
Cytokines	Monoclonal antibodies	Suppress inflammatory signaling and reduce neuroinflammation
Microglia	Neuroprotective drugs	Prevent excessive activation and protect neurons from damage
Toll-like receptors	Receptor antagonists	Inhibit immune activation and reduce inflammatory cascades

9. Microbiome-Based Therapeutic Approaches:

Recent advances in biomedical research have highlighted the importance of targeting the Gut microbiota as a potential strategy for managing neuroinflammatory and neurodegenerative disorders. Because the gut microbiota plays a key role in regulating immune responses, metabolism, and neural communication, therapeutic interventions that modify microbial composition have gained significant attention. These approaches aim to restore microbial balance, reduce systemic inflammation, and improve gut–brain communication within the Gut–brain–immune axis. Several microbiome-based therapies, including probiotics, prebiotics, synbiotics, dietary interventions, and fecal microbiota transplantation, are currently being explored for their potential benefits in neurological health [31, 34, 39].

9.1. Probiotics-

Probiotics are live microorganisms that provide health benefits to the host when administered in adequate amounts. These beneficial microbes help restore microbial balance within the gastrointestinal tract and may contribute to improved immune regulation. Probiotics can enhance intestinal barrier function, inhibit the growth of pathogenic microorganisms, and promote the production of anti-inflammatory metabolites. Through these mechanisms, probiotics may help reduce systemic inflammation and modulate neuroinflammatory processes associated with neurological disorders [31, 36].

9.2. Prebiotics-

Prebiotics are non-digestible dietary components that selectively stimulate the growth and activity of beneficial gut bacteria. Common prebiotics include dietary fibers and certain oligosaccharides that serve as substrates for microbial fermentation. The fermentation process leads to the production of beneficial metabolites such as Short-chain fatty acids, which play an important role in maintaining intestinal barrier integrity and regulating immune responses. By supporting beneficial microbial populations, prebiotics may help improve gut health and reduce inflammatory signaling linked to neuroinflammation [11, 31].

9.3. Synbiotics-

Synbiotics refer to a combination of probiotics and prebiotics designed to enhance the survival and activity of beneficial microorganisms within the gut. This combined approach provides both beneficial microbes and the nutrients required for their growth. Synbiotic formulations may produce synergistic effects by improving microbial diversity, enhancing metabolic activity, and strengthening immune regulation. As a result, synbiotics are increasingly being investigated for their potential role in improving neurological health and reducing inflammatory responses [34].

9.4. Dietary Interventions-

Diet plays a crucial role in shaping the composition and metabolic activity of gut microbiota. Dietary interventions that include high-fiber foods, plant-based nutrients, and fermented products can promote the growth of beneficial microorganisms and support microbial diversity. Nutritional components such as polyphenols, antioxidants, and omega-3 fatty acids may also contribute to anti-inflammatory effects and improved neural health. Through modulation of microbial composition and metabolic pathways, dietary strategies can influence the gut–brain axis and potentially reduce the risk of neuroinflammatory disorders [31, 35].

9.5. Fecal Microbiota Transplantation-

Fecal microbiota transplantation (FMT) is an emerging therapeutic technique that involves the transfer of processed stool from a healthy donor into the gastrointestinal tract of a recipient. The goal of this procedure is to restore a healthy microbial community and correct dysbiosis. By reintroducing beneficial microorganisms, FMT may help reestablish microbial diversity, improve intestinal barrier function, and reduce inflammatory responses. Although research in neurological disorders is still developing, early studies suggest that FMT may have potential benefits in conditions associated with gut microbiota imbalance [39].

Table 3. Microbiome-Based Interventions in Neuroinflammatory Diseases

Therapy	Mechanism	Clinical Outcome
Probiotics	Restoration of microbial balance and inhibition of pathogenic bacteria	Reduction in systemic inflammation and improved gut health
Prebiotics	Stimulation of beneficial bacteria and increased short-chain fatty acid production	Strengthening of intestinal barrier and improved immune regulation
Fecal microbiota transplantation	Restoration of healthy microbial community	Improvement in neurological symptoms and reduction in gut dysbiosis

10. Natural Products and Herbal Compounds Targeting the Axis:

Natural products and medicinal plants have historically served as a rich source of therapeutic agents for diverse diseases. In recent years, research has increasingly focused on plant-derived bioactive compounds capable of modulating the Gut–brain–immune axis. Many phytochemicals possess anti-inflammatory, antioxidant, and neuroprotective properties, which may help regulate gut microbiota composition, reduce neuroinflammatory signaling, and enhance neural function. Due to their generally low toxicity and multifaceted biological activities, these natural compounds are being actively explored as complementary therapies for neurological disorders [12, 31, 40].

10.1 Curcumin-

Curcumin, a polyphenolic compound extracted from Curcuma longa, has garnered significant attention for its therapeutic potential. It exhibits strong anti-inflammatory and antioxidant activities and can modulate multiple molecular pathways implicated in neuroinflammation. Curcumin has been reported to inhibit pro-inflammatory cytokine production, reduce oxidative stress, and improve intestinal barrier integrity. Furthermore, curcumin may influence gut microbial composition by promoting beneficial bacterial populations, thereby contributing to improved gut–brain signaling [12, 31].

10.2 Polyphenols-

Polyphenols, widely found in plant-based foods and medicinal herbs, are potent antioxidant compounds with immunomodulatory properties. They can affect microbial metabolism in the gastrointestinal tract and mitigate oxidative stress and inflammatory responses. Through these mechanisms, polyphenols may support neuronal health and enhance communication along the gut–brain axis, making them valuable candidates for dietary interventions in neuroinflammatory disorders [31,35].

10.3 Withania somnifera (Ashwagandha)-

Withania somnifera, commonly known as Ashwagandha, is an adaptogenic herb extensively used in traditional medicine. Its bioactive constituents, Withanolides, exhibit neuroprotective, anti-inflammatory, and stress-modulating effects. These compounds may regulate immune responses and support neuronal function, positioning Ashwagandha as a promising natural therapy for neuroinflammatory and neurodegenerative conditions [12, 40].

10.4 Camellia sinensis (Green Tea)-

Green tea (Camellia sinensis) contains bioactive catechins with potent antioxidant activity. Catechins have been shown to reduce oxidative damage in neural tissues and modulate gut microbiota composition, promoting beneficial microbial populations. Through these combined effects, catechins may enhance metabolic and immune balance, contributing to improved gut–brain communication [31, 35].

Overall, herbal compounds and plant-derived bioactive molecules represent a valuable therapeutic avenue for modulating gut microbiota, regulating immune responses, and protecting neural tissues from inflammation. Ongoing pharmacological research into natural products may facilitate the development of novel interventions targeting the gut–brain–immune axis for the prevention and management of neuroinflammatory disorders [12, 31, 40].

Table 4. Herbal Modulators of the Gut–Brain Axis

Herb	Active Compound	Mechanism
Withania somnifera	Withanolides	Neuroprotective activity and modulation of stress-related pathways
Curcuma longa	Curcumin	Anti-inflammatory and antioxidant effects
Camellia sinensis	Catechins	Antioxidant activity and regulation of gut microbial balance

11. Experimental Models for Studying the Gut–Brain Axis:

Understanding the complex interactions within the Gut–brain axis requires the use of advanced experimental models and analytical techniques. Researchers employ a variety of biological, molecular, and imaging methods to investigate how gut microbiota influences immune responses and brain function. These experimental approaches allow scientists to examine microbial composition, immune signaling pathways, neurological behavior, and structural changes in the brain. Together, these models provide valuable insights into the mechanisms linking gut microbiota with neuroinflammation and neurological disorders [1, 4, 9].

11.1 Germ-Free Animal Models-

One of the most widely used experimental systems in gut–brain axis research is the Germ-free animal model. These animals are raised in sterile environments and lack any microorganisms in their gastrointestinal tract. Because of the absence of gut microbiota, germ-free animals provide a unique opportunity to study the direct influence of microbial communities on physiological and neurological processes. Studies using germ-free models have shown that the absence of gut microbes can significantly affect immune system development, brain chemistry, and behavior. When specific microbial strains are introduced into these animals, researchers can observe how microbial colonization influences neural signaling, inflammation, and cognitive functions. These models therefore play a critical role in identifying causal relationships between gut microbiota and neurological health [1, 5, 7, 32].

11.2 Microbiome Sequencing Techniques-

Modern molecular techniques allow researchers to analyze the diversity and composition of microbial communities present in the gastrointestinal tract. One of the most commonly used methods is 16S rRNA sequencing, which enables identification and classification of bacterial species based on genetic markers. This technique provides detailed information about microbial diversity and abundance within the gut ecosystem. By comparing microbial profiles from healthy and diseased individuals, researchers can identify microbial alterations associated with neuroinflammatory disorders. Microbiome sequencing therefore plays a crucial role in understanding how microbial imbalance contributes to disease development [11, 31, 34].

11.3 Behavioral Neurological Tests-

Behavioral assessments are also essential tools for evaluating the functional effects of gut microbiota on brain activity. Various experimental tests are used to measure cognitive performance, emotional responses, and motor behavior in animal models. These tests help researchers determine how changes in gut microbial composition influence neurological functions such as learning, memory, anxiety, and stress responses.

Behavioral studies provide important evidence linking gut microbial alterations with neurological outcomes. When combined with molecular and immunological analyses, these experiments offer a comprehensive understanding of gut–brain interactions [6, 32].

11.4 Neuroimaging Studies-

Advanced imaging techniques are increasingly used to investigate structural and functional changes in the brain associated with neuroinflammation. One important imaging method is Magnetic resonance imaging, which allows non-invasive visualization of brain tissues.

Neuroimaging studies can detect inflammation, structural abnormalities, and changes in neural connectivity within the central nervous system. These imaging approaches help researchers examine how gut microbiota-related immune responses affect brain structure and function. Such techniques provide valuable clinical and experimental insights into neurological disorders associated with gut–brain axis dysregulation [8, 14, 19].

Table 5. Experimental Techniques Used in Gut–Brain Axis Research

Technique	Application
16S rRNA sequencing	Profiling and identification of gut microbial communities
ELISA	Detection and quantification of cytokines and inflammatory mediators
Western blot	Analysis of protein expression involved in inflammatory and signaling pathways
MRI	Imaging of brain inflammation and structural changes

12.Clinical Trials and Translational Research:

The growing recognition of the Gut–brain–immune axis has stimulated considerable interest in translating basic scientific discoveries into clinical applications. In recent years, several clinical investigations have explored microbiome-based

therapeutic strategies aimed at reducing neuroinflammation and improving neurological health. These studies focus on understanding how modulation of the Gut microbiota may influence disease progression and treatment outcomes in various neurological disorders [15, 24, 26].

12.1 Ongoing Clinical Studies-

A number of ongoing clinical trials are evaluating the effectiveness of microbiome-targeted therapies such as probiotics, prebiotics, dietary interventions, and Fecal microbiota transplantation. These studies aim to determine whether restoring microbial balance can reduce inflammatory responses and improve neurological symptoms in patients with disorders associated with neuroinflammation. Clinical investigations have particularly focused on diseases such as Alzheimer's disease, Parkinson's disease, Multiple sclerosis, and Major depressive disorder. Early findings suggest that microbiome modulation may influence immune signaling, metabolic activity, and neural communication pathways. Some clinical trials have reported improvements in inflammatory markers, cognitive performance, and gastrointestinal health following microbiome-based interventions. However, the results are still evolving, and larger well-controlled studies are required to confirm the therapeutic benefits of these approaches [15, 24, 32].

12.2 Therapeutic Limitations-

Despite promising preliminary results, several therapeutic limitations remain in the clinical application of microbiome-based treatments. One major challenge is the variability in microbial composition among individuals, which can influence treatment responses. Differences in genetics, diet, lifestyle, and environmental exposure may significantly affect gut microbial diversity [15, 36, 38]. Another limitation involves the lack of standardized protocols for microbiome-based therapies. For example, probiotic formulations, dosing regimens, and treatment duration may vary between studies. Similarly, the long-term safety and efficacy of fecal microbiota transplantation require further investigation. These factors highlight the need for standardized clinical guidelines and rigorous clinical evaluation.

12.3 Translational Challenges-

Translating experimental findings from laboratory research into effective clinical therapies presents additional challenges. Many mechanistic insights have been derived from animal models, which may not fully replicate the complexity of human physiology. Therefore, translating these findings into clinical practice requires careful validation through human studies. Furthermore, identifying specific microbial species or metabolites responsible for therapeutic effects remains an ongoing area of investigation. Advances in microbiome sequencing technologies, biomarker identification, and personalized medicine approaches may help overcome these challenges. Continued collaboration between basic researchers, clinicians, and pharmaceutical scientists will be essential for developing effective microbiome-targeted therapies [1, 4, 12, 17, 31].

International Journal of Science, Strategic Management and Technology
Volume **02** Issue **03** March-**2026** | ISSN: **3108-1762 (Online)** | Impact Factor: 3.8
An International, Peer-Reviewed, Open Access Scholarly Journal Indexed in recognized academic databases

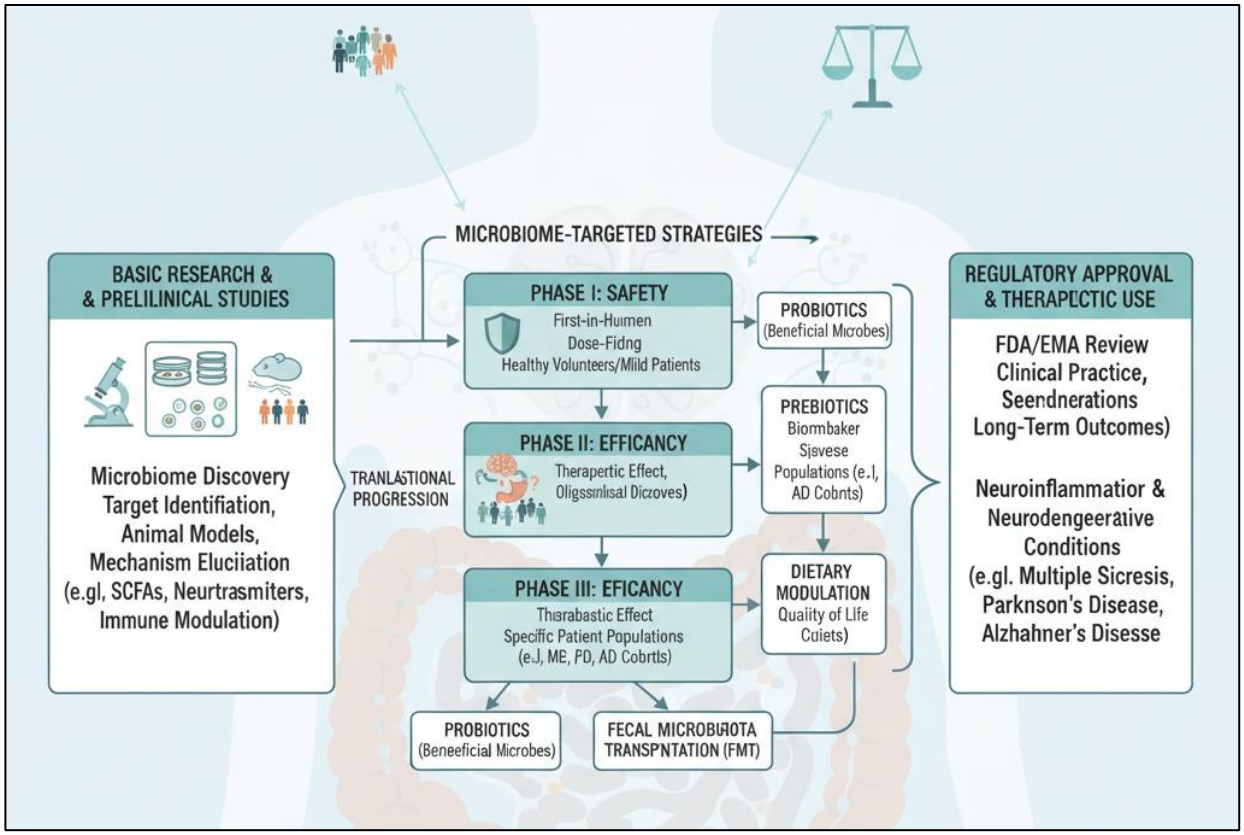

Figure 6: Clinical trial pipeline for microbiome-based therapies.

(A conceptual flow diagram illustrating the stages involved in the development of microbiome-based therapies targeting neuroinflammatory disorders. The figure should depict the progression from basic research and preclinical studies, through clinical trial phases (Phase I, Phase II, and Phase III), to regulatory approval and clinical application. The diagram may also include examples of therapeutic strategies such as probiotics, dietary interventions, and fecal microbiota transplantation within the clinical development pipeline.)

13. Future Perspectives and Emerging Technologies:

Research on the Gut–brain–immune axis is rapidly expanding, and several emerging technologies are expected to transform the way neuroinflammatory disorders are diagnosed and treated. Advances in microbiome science, computational biology, and precision medicine are opening new opportunities for the development of innovative therapeutic strategies targeting gut–brain communication [1, 4, 9, 12].

13.1 Personalized Microbiome Therapy-

One of the most promising future directions is the development of personalized microbiome-based therapies. Since the composition of the Gut microbiota varies significantly among individuals, personalized approaches aim to design treatment strategies based on a patient's unique microbial profile. Such therapies may include customized probiotic formulations, dietary recommendations, or targeted microbial interventions designed to restore microbial balance and reduce inflammation. Personalized microbiome therapy may improve treatment outcomes by addressing individual variations in microbial composition, metabolic activity, and immune responses. This approach aligns with the broader concept of precision medicine, where therapeutic strategies are tailored to the biological characteristics of each patient [12, 31, 36].

13.2 AI-Based Microbiome Analysis-

The application of Artificial Intelligence and advanced computational tools is playing an increasingly important role in microbiome research. AI-based analytical systems can process large datasets generated from microbiome sequencing technologies and identify patterns associated with disease states. Machine learning algorithms can help predict disease risk, identify microbial biomarkers, and guide therapeutic decision-making. By integrating microbiome data with clinical, genetic, and metabolic information, AI-based platforms may significantly improve our understanding of complex interactions within the gut–brain–immune network [12, 31, 34].

13.3 Microbiome-Derived Pharmaceuticals-

Another emerging area of research involves the development of microbiome-derived pharmaceuticals. Certain microbial metabolites and bioactive compounds produced by gut microorganisms may possess significant therapeutic potential [11, 34]. For example, microbial metabolites such as Short-chain fatty acids play important roles in regulating immune responses, maintaining intestinal barrier integrity, and modulating neural signaling. Future drug discovery efforts may focus on isolating and synthesizing microbiome-derived molecules that can be used as targeted pharmacological agents for the treatment of neuroinflammatory and neurodegenerative diseases [12, 31].

13.4 Biomarker Discovery-

Identifying reliable biomarkers is essential for early diagnosis, disease monitoring, and therapeutic evaluation. Microbiome-based biomarkers may include specific bacterial species, microbial metabolites, or inflammatory mediators that are associated with disease progression. Advances in microbiome sequencing, metabolomics, and systems biology may facilitate the discovery of novel biomarkers linked to neuroinflammatory conditions. These biomarkers could help clinicians assess disease risk, evaluate treatment responses, and design personalized therapeutic interventions 12, 31, 34].

14. Conclusion:

The Gut–brain–immune axis represents a complex and dynamic communication network connecting the gastrointestinal microbiota, immune system, and central nervous system. Increasing scientific evidence highlights the critical role of gut microbial communities in regulating immune responses and influencing neuroinflammatory processes associated with various neurological disorders. Disruptions in gut microbial balance can contribute to immune dysregulation, inflammatory signaling, and neuronal damage, thereby playing a significant role in the development of several neurodegenerative and neuropsychiatric conditions. Understanding these interactions has opened new avenues for pharmacological intervention aimed at modulating gut microbiota and associated immune pathways. Microbiome-based therapeutic strategies, including probiotics, dietary modulation, and microbiota transplantation, have demonstrated promising potential in experimental and clinical research. Furthermore, advances in personalized medicine, artificial intelligence-based microbiome analysis, and microbiome-derived pharmaceuticals may significantly enhance future treatment strategies. Overall, targeting the gut–brain–immune axis offers an innovative and promising approach for the prevention and management of neuroinflammatory diseases. Continued interdisciplinary research integrating microbiology, immunology, neuroscience, and pharmacology will be essential to translate these discoveries into effective clinical therapies.

15. References:

[1] Cryan JF, O'Riordan KJ, Cowan CSM, Sandhu KV, Bastiaanssen TFS, Boehme M, et al. The microbiota–gut–brain axis. Physiol Rev. 2019;99(4):1877–2013.
[2] Sharon G, Sampson TR, Geschwind DH, Mazmanian SK. The central nervous system and the gut microbiome. Cell. 2016;167(4):915–932.
[3] Carabotti M, Scirocco A, Maselli MA, Severi C. The gut–brain axis: interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol. 2015;28(2):203–209.
[4] Fung TC, Olson CA, Hsiao EY. Interactions between the microbiota, immune and nervous systems in health and disease. Nat Neurosci. 2017;20(2):145–155.
[5] Sampson TR, Mazmanian SK. Control of brain development, function, and behavior by the microbiome. Cell Host Microbe. 2015;17(5):565–576.
[6] Quigley EMM. Microbiota–brain–gut axis and neurodegenerative diseases. Curr Neurol Neurosci Rep. 2017;17(12):94.
[7] Dinan TG, Cryan JF. Gut instincts: microbiota as a key regulator of brain development, ageing and neurodegeneration. J Physiol. 2017;595(2):489–503.
[8] Mayer EA, Knight R, Mazmanian SK, Cryan JF, Tillisch K. Gut microbes and the brain: paradigm shift in neuroscience. J Neurosci. 2014;34(46):15490–15496.
[9] Morais LH, Schreiber HL, Mazmanian SK. The gut microbiota–brain axis in behaviour and brain disorders. Nat Rev Microbiol. 2021;19(4):241–255.
[10] Cryan JF, Dinan TG. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. Nat Rev Neurosci. 2012;13(10):701–712.
[11] Dalile B, Van Oudenhove L, Vervliet B, Verbeke K. The role of short-chain fatty acids in microbiota–gut–brain communication. Nat Rev Gastroenterol Hepatol. 2019;16(8):461–478.
[12] Parker A, Fonseca S, Carding SR. Gut microbes and metabolites as modulators of blood–brain barrier integrity and brain health. Gut Microbes. 2020;11(2):135–157.
[13] Foster JA, Neufeld KM. Gut–brain axis: how the microbiome influences anxiety and depression. Trends Neurosci. 2013;36(5):305–312.
[14] Braniste V, Al-Asmakh M, Kowal C, Anuar F, Abbaspour A, Tóth M, et al. The gut microbiota influences blood–brain barrier permeability in mice. Sci Transl Med. 2014;6(263):263ra158.
[15] Vendrik KEW, Ooijevaar RE, de Jong PRC, Laman JD, van Oosten BW, van Hilten JJ, et al. Fecal microbiota transplantation in neurological disorders. Front Cell Infect Microbiol. 2020;10:98.
[16] Dinan TG, Stanton C, Cryan JF. Psychobiotics: a novel class of psychotropic. Biol Psychiatry. 2013;74(10):720–726.
[17] Rutsch A, Kantsjö JB, Ronchi F. The gut–brain axis: how microbiota and host inflammasome influence brain physiology and pathology. Front Immunol. 2020;11:604179.
[18] Mohajeri MH, Brummer RJM, Rastall RA, Weersma RK, Harmsen HJM, Faas M, et al. The role of the microbiome for human health: from basic science to clinical applications. Eur J Nutr. 2018;57(Suppl 1):1–14.
[19] Mayer EA. Gut feelings: the emerging biology of gut–brain communication. Nat Rev Neurosci. 2011;12(8):453–466.
[20] Wang HX, Wang YP. Gut microbiota–brain axis. Chin Med J. 2016;129(19):2373–2380.
[21] Collins SM, Surette M, Bercik P. The interplay between the intestinal microbiota and the brain. Nat Rev Microbiol. 2012;10(11):735–742.
[22] Galland L. The gut microbiome and the brain. J Med Food. 2014;17(12):1261–1272.
[23] Ochoa-Repáraz J, Kasper LH. The second brain: is the gut microbiota a link between obesity and central nervous system disorders? Curr Obes Rep. 2016;5(1):51–64.
[24] Tremlett H, Bauer KC, Appel-Cresswell S, Finlay BB, Waubant E. The gut microbiome in human neurological disease. Ann Neurol. 2017;81(3):369–382.

[25] Mulak A, Bonaz B. Brain–gut–microbiota axis in Parkinson's disease. World J Gastroenterol. 2015;21(37):10609–10620.
[26] Vogt NM, Kerby RL, Dill-McFarland KA, Harding SJ, Merluzzi AP, Johnson SC, et al. Gut microbiome alterations in Alzheimer's disease. Sci Rep. 2017;7:13537.
[27] Berer K, Krishnamoorthy G. Microbial view of central nervous system autoimmunity. FEBS Lett. 2014;588(22):4207–4213.
[28] Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. Cell. 2014;157(1):121–141.
[29] Erny D, Hrabě de Angelis AL, Prinz M. Communicating systems in the body: how microbiota and microglia cooperate. Immunity. 2017;46(6):938–952.
[30] Sampson TR, Debelius JW, Thron T, Janssen S, Shastri GG, Ilhan ZE, et al. Gut microbiota regulate motor deficits and neuroinflammation in a model of Parkinson's disease. Cell. 2016;167(6):1469–1480.
[31] Nicholson JK, Holmes E, Kinross J, Burcelin R, Gibson G, Jia W, et al. Host–gut microbiota metabolic interactions. Science. 2012;336(6086):1262–1267.
[32] Zheng P, Zeng B, Liu M, Chen J, Pan J, Han Y, et al. The gut microbiome from patients with major depressive disorder modulates depressive-like behaviors. Sci Transl Med. 2016;8(341):341ra75.
[33] Cryan JF, O'Mahony SM. The microbiome–gut–brain axis: from bowel to behavior. Neurogastroenterol Motil. 2011;23(3):187–192.
[34] De Vadder F, Kovatcheva-Datchary P, Goncalves D, Vinera J, Zitoun C, Duchampt A, et al. Microbiota-generated metabolites promote metabolic benefits via gut–brain neural circuits. Cell. 2014;156(1–2):84–96.
[35] Westfall S, Lomis N, Kahouli I, Dia SY, Singh SP, Prakash S. Microbiome, probiotics and neurodegenerative diseases. Neural Regen Res. 2017;12(5):681–686.
[36] Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. Probiotics and prebiotics in intestinal health and disease. Nat Rev Gastroenterol Hepatol. 2019;16(10):605–616.
[37] Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document: probiotics definition and scope. Nat Rev Gastroenterol Hepatol. 2014;11(8):506–514.
[38] Peterson CT, Sharma V, Elmen L, Peterson SN. Immune homeostasis, dysbiosis and therapeutic modulation of the gut microbiota. Clin Exp Immunol. 2015;179(3):363–377.
[39] Cryan JF, O'Riordan KJ, Sandhu K, Peterson V, Dinan TG. The gut microbiome in neurological disorders. Lancet Neurol. 2020;19(2):179–194.
[40] Dinan TG, Cryan JF. Regulation of the stress response by the gut microbiota: implications for psychoneuroendocrinology. Psychoneuroendocrinology. 2017;83:3–10.