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REVIEW ARTICLE

The Role of Gut-Derived Neurotransmitters in the Pathogenesis of Autoimmune Neurological Disorders

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Abstract

Autoimmune neurological disorders such as multiple sclerosis, myasthenia gravis, neuromyelitis optica spectrum disorders (NMOSD), and stiff-person syndrome (SPS) result from dysregulated immune responses targeting central nervous system (CNS) components. Emerging evidence highlights the gut–brain axis as a key modulator of neuroimmunological health, with gut-derived neurotransmitters acting as critical mediators linking the gut microbiome, mucosal immunity, and CNS autoimmunity. In this review, we explore current knowledge on how gut-derived serotonin (5-HT), γ-aminobutyric acid (GABA), dopamine, acetylcholine, and related metabolites influence immune cell function and contribute to the pathogenesis of autoimmune neurological diseases. We discuss the mechanisms by which microbial communities regulate neurotransmitters production, the pathways through which these neurotransmitter modulate peripheral and central immune responses, and how dysbiosis or altered neurotransmitter signaling may promote neuroinflammation and autoimmunity. Specifically, we examine the roles of 5-HT in suppressing Th17 responses in multiple sclerosis, GABA in T cell regulation, dopamine in modulating IL-17 and microglial activation, and cholinergic signaling in gut immune homeostasis. We also explore the contribution of microbial metabolites short-chain fatty acids and bile acids that influence neurotransmitter release and immune tolerance. Finally, we highlight potential translational avenues, including neurotransmitter modulating probiotics, dietary interventions, and pharmacotherapies targeting gut neurotransmission. Understanding these pathways may open preventive and therapeutic strategies in autoimmune neurological disorders by harnessing gut-CNS immunomodulation.

1. Introduction

The human gut is an intricate ecosystem of microorganisms that not only participate in nutrient digestion but also exert a profound influence on neurodevelopment, behavior, and immune function. Over the past decade, the bidirectional communication axis between the gut and the brain termed the gut-brain axis has emerged as a critical pathway linking gastrointestinal health to central nervous system (CNS) homeostasis (Arneth, 2018). An increasingly appreciated aspect of this axis is the role of gut-derived neurotransmitters, such as serotonin, gamma-aminobutyric acid (GABA), dopamine, and histamine, in modulating neuroimmune interactions. These bioactive molecules, largely synthesized by gut microbiota or enteroendocrine cells (Chen et al., 2022), have systemic immunological implications and are believed to play pivotal roles in the onset and progression of autoimmune neurological disorders.

Autoimmune neurological disorders, including multiple sclerosis, neuromyelitis optica spectrum disorder (NMOSD), autoimmune encephalitis, and myasthenia gravis, are characterized by the immune system's aberrant attack on neuronal components. While the etiology of these conditions is multifactorial, mounting evidence supports the concept that gut microbiota and their metabolites including neurotransmitters can modulate systemic inflammation, breach the blood-brain barrier, and activate autoreactive lymphocytes (Oshaghi et al., 2023). More than 90% of the body's serotonin is synthesized in the gastrointestinal tract and that GABA and dopamine production is significantly influenced by microbial populations such as Lactobacillus,

Bifidobacterium, and Escherichia coli (Legan et al., 2022; Liu et al., 2020), the gut is increasingly being recognized as a potent neuroendocrine organ.

Gut-derived neurotransmitters exert immunomodulatory effects by acting on immune cells, including T cells, B cells, and dendritic cells, altering their phenotype and cytokine profiles. For example, serotonin can influence T helper cell differentiation and interleukin production, while GABA has been shown to suppress proinflammatory responses and induce regulatory T cell activity (Shajib and Khan, 2015; Wan et al., 2020). These interactions are particularly relevant in autoimmune settings where immune tolerance is broken. Additionally, neurotransmitter imbalances may indirectly shape CNS autoimmunity by altering intestinal permeability, enabling microbial products and immune cells to access systemic circulation and prime inflammatory responses. Recent studies utilizing germ-free animal models and fecal microbiota transplantation techniques have further illustrated the gut microbiota's influence on neuroinflammatory pathways (Zhao et al., 2021). Disruption in microbial populations has been shown to exacerbate experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis, while supplementation with certain probiotics or prebiotics has resulted in amelioration of disease symptoms. These findings suggest that gut-derived neurotransmitters serve not merely as signaling molecules but as critical mediators of immune homeostasis at the gut-brain interface.

2. Gut-Derived Neurotransmitters and Their Microbial Origins

2.1 Serotonin (5-Hydroxytryptamine, 5-HT)

Serotonin (5-HT), a key neurotransmitter involved in mood regulation, gastrointestinal motility, and immune modulation, is predominantly synthesized in the gastrointestinal tract (Guzel and Mirowska-Guzel, 2022), where approximately 90% of the body's total serotonin is produced. The primary producers are enterochromaffin cells, a subtype of enteroendocrine cells within the intestinal lining. The synthesis of serotonin in the gut is tightly regulated by dietary tryptophan availability and significantly influenced by the metabolic activity of the gut microbiota. Specific bacterial species such as *Turicibacter sanguinis, Clostridium ramosum*, and members of the Enterococcus genus have been shown to modulate host tryptophan metabolism and influence serotonin biosynthesis via short-chain fatty acid production, notably butyrate. These microbial products stimulate the expression of tryptophan hydroxylase 1, the rate-limiting enzyme for serotonin synthesis in the gut (O'Mahony et al., 2015; Wang et al., 2023).

In the context of autoimmune neurological disorders, especially multiple sclerosis, dysregulation of the serotonergic system has been reported. Patients with multiple sclerosis exhibit altered serum and cerebrospinal fluid levels of serotonin, along with differential expression of serotonin transporters and receptors (Hesse et al., 2014), suggesting a link between serotonergic signaling and disease activity. In experimental autoimmune encephalomyelitis, the mouse model of multiple sclerosis, elevated gut-derived serotonin has been observed to exert immunosuppressive effects (Correale et al., 2022). Mechanistically, serotonin reduces the production of proinflammatory cytokines such as IL-17 and IFN-γ, both of which are central to Th17-mediated autoimmunity in multiple sclerosis (Sales et al., 2021). These findings highlight the potential role of gut-derived serotonin as a modulator of peripheral immune tolerance and a promising target in neuroimmune therapeutics.

2.2 γ-Aminobutyric Acid

GABA, or γ-aminobutyric acid, is the principal inhibitory neurotransmitter in the CNS, known for regulating neuronal excitability and maintaining synaptic balance. Beyond its well-established neural role, GABA is also produced in the gut by several commensal bacterial species. Notably, Lactobacillus brevis, *Bifidobacterium dentium, Lactobacillus plantarum*, and *Escherichia coli* have been identified as microbial sources of GABA (Pokusaeva et al., 2017; Yunes et al., 2016) (Table 1). These bacteria possess the glutamate decarboxylase system, which enables them to convert glutamate into GABA. This microbial GABA can cross the gut epithelium and enter systemic circulation, potentially influencing immune cells that express GABA receptors, including T lymphocytes, macrophages, and dendritic cells (Bhandage and Barragan, 2021).

GABA exerts multiple immunomodulatory effects, acting through both GABAA and GABAB receptor subtypes. In autoimmune conditions like multiple sclerosis, GABAergic signaling has been shown to suppress T cell proliferation and inflammatory cytokine production. Animal models of autoimmune encephalomyelitis have demonstrated that oral or systemic administration of GABA reduces disease severity, delays symptom onset, and modulates the balance of effector T cells and regulatory T cells (Carmans et al., 2013). Specifically, GABA suppresses Th1 and Th17 responses, key drivers of autoimmune pathology in the CNS (Bhat et al., 2010). Additionally, GABA enhances Treg populations and inhibits antigen-presenting cell activity. Thus, microbial GABA production represents a novel pathway through which the gut microbiota may influence systemic autoimmunity and neuroinflammation.

2.3 Dopamine

Dopamine, a catecholamine neurotransmitter involved in reward signalling, motor control, and endocrine regulation, is also synthesized by gut-resident bacteria (Kasarello et al., 2023). Species such as *Bacillus spp., Escherichia coli, Proteus mirabilis*, and *Staphylococcus aureus* are capable of producing dopamine from dietary L-dopa via enzymatic decarboxylation. Dopaminergic signalling in the periphery is increasingly recognized as a modulator of immune function. Dopamine receptors, particularly D1-like and D2-like receptors, are expressed on various immune cells, including T cells, B cells, monocytes, and dendritic cells (Levite, 2016), where they modulate intracellular cAMP levels and alter cytokine production (Table 2).

In multiple sclerosis and other autoimmune neurological disorders, perturbations in dopamine levels have been observed, especially during active disease phases. Dopamine appears to exert dose and receptor-specific effects: low concentrations generally enhance inflammatory responses via D1 receptors, while higher concentrations tend to be anti-inflammatory via D2-like receptors. Experimental data indicate that dopamine downregulates IL-17 production and promotes regulatory T cell development. Moreover, dopamine

influences blood-brain barrier permeability, a critical factor in the initiation and progression of CNS autoimmunity (Williams and Klein, 2017). The link between microbial dopamine production and neuroimmune modulation is still emerging, but evidence suggests that manipulating gut microbial composition could influence systemic dopamine levels and, consequently, immune responses. Given the bidirectional transport of dopamine precursors between the gut and brain, gut-derived dopamine may be a crucial intermediary in neuroimmune crosstalk.

2.4 Acetylcholine and Other Neurotransmitters

Acetylcholine (ACh), traditionally considered a neuronal neurotransmitter, is also synthesized by non-neuronal sources including gut epithelial cells, immune cells, and certain gut bacteria such as *Lactobacillus plantarum.* The non-neuronal cholinergic system plays a vital role in maintaining intestinal barrier integrity and immune homeostasis. ACh acts via muscarinic and nicotinic receptors on a variety of immune cells, including dendritic cells, T cells, and macrophages (Kawashima et al., 2012). The cholinergic anti-inflammatory pathway mediated by vagal stimulation and nicotinic acetylcholine receptors, inhibits the release of proinflammatory cytokines such as TNF-α, IL-6, and IL-1β. Dysregulation of cholinergic signaling has been implicated in several autoimmune conditions, including multiple sclerosis and systemic lupus erythematosus. Experimental data show that activation of cholinergic pathways can suppress autoimmune encephalomyelitis severity by dampening neuroinflammatory responses. Although research on microbial regulation of acetylcholine is still in its infancy, emerging studies suggest that microbiota-driven changes in ACh synthesis or degradation may impact mucosal immunity and systemic inflammatory status (Macpherson et al., 2023).

Other neurotransmitters, including norepinephrine and histamine, also have microbial origins or can be influenced by gut flora. Certain strains of *Enterococcus faecalis* and *Escherichia coli* produce norepinephrine, while *Lactobacillus reuteri* and *Morganella morganii* are known to produce histamine (Fiorani et al., 2023). Both neurotransmitters influence gut motility, barrier function, and immune modulation. Histamine, in particular, can activate H1-H4 receptors on immune cells and is associated with both pro- and anti-inflammatory effects depending on the context. In autoimmune neurological disorders, alterations in histamine signaling have been linked with blood-brain barrier disruption and CNS inflammation (Yue et al., 2023).

Table 1: Probiotic strains which modulate neurotransmitter levels and their potential immunomodulatory roles

Probiotic Strain	Neurotransmitter Affected	Mechanism of Action	Immune Modulation Observed	Implications in Autoimmune Neurological Disorders
Lactobacillus rhamnosus JB-1	GABA	Upregulates GABA receptor expression in CNS; enhances GABA production	Increases Tregs; reduces pro-inflammatory cytokines	May reduce neuroinflammation in MS and SPS
Bifidobacterium infantis 35624	Serotonin	Increases tryptophan availability; affects serotonin synthesis in gut	Decreases TNF-α and IFN-γ; improves IL-10 production	Could modulate Th1/Th17 in MS
Lactobacillus plantarum PS128	Dopamine	Enhances dopamine biosynthesis via microbial tyrosine decarboxylation	Alters microglial activation; balances Th1/Th2 responses	Potential benefit in MS and Parkinson-like neuroimmune overlap
Bacteroides fragilis	Acetylcholine	Indirect effect via polysaccharide A (PSA); enhances vagal tone and ACh release	Promotes Treg development; reduces CNS-infiltrating Th17 cells	Shown to reverse EAE severity in mouse models
Escherichia coli Nissle 1917	Multiple (DA, NE, 5-HT)	Produces biogenic amines; modulates neurotransmitter synthesis pathways	Balances immune cell migration and barrier integrity	May stabilize gut-brain immune axis

Table 2: Gut-Derived Neurotransmitter Influence on Key Immune Cells in Autoimmune Neurological Disorders

Neurotransmitter	Primary Immune Cell Targets	Receptors Involved	Immunological Effect	Impact on Autoimmune Neurological Disorders
Serotonin (5HT)	$CD4^+$ T cells, Dendritic cells	5HT1A, 5HT2A, 5HT7	Suppresses Th17/Th1, enhances IL-10 via DCs	Dampens proinflammatory T cell responses in MS
GABA	T cells, Macrophages	GABAA, GABAB	Reduces IL17/IFNγ, increases $Foxp3^+$ Tregs, inhibits antigen presentation	Restores immune tolerance in MS, T1D, SPS
Dopamine	T cells, Microglia	D1-like (DRD1, DRD5), D2-like	D2-like → Treg induction; D1-like → Th17 promotion at low levels	Balances neuroinflammation in relapsing MS and CNS autoimmunity
Acetylcholine (ACh)	Macrophages, T cells	α7nAChR, M3	α7nAChR activation inhibits TNFα/IL6; maintains epithelial barrier	Reduces systemic inflammation; enhances BBB integrity
Histamine	Mast cells, T cells, B cells	H1–H4 receptors	H2/H4 promote immune suppression; H1 promotes inflammation depending on local context	Underexplored in MS/ NMOSD but linked to BBB breakdown and inflammatory bias

3. Immunomodulatory Actions of Gut-Derived Neurotransmitters

3.1 Serotonin's Effects on Immune Cells

Although serotonin was classically recognized as a neurotransmitter with central roles in mood regulation, also exerts substantial immunomodulatory effects in the periphery. In the gut, serotonin is predominantly synthesized by enterochromaffin cells in response to microbial metabolites such as short-chain fatty acids (SCFAs) and dietary tryptophan availability (Reigstad et al., 2015). Immune cells including macrophages, dendritic cells, and lymphocytes express serotonin receptors, through which serotonin can influence their activation state and cytokine production. Notably, serotonin has been shown to attenuate the expression of major histocompatibility complex class II molecules on antigen-presenting cells (Branco-de-Almeida et al., 2011), thereby reducing their capacity to activate naïve T cells. Furthermore, serotonin can downregulate the production of pro-inflammatory cytokines such as IL-6 and TNF-α, which are central to the pathology of many autoimmune diseases including multiple sclerosis. Serotonin suppresses the differentiation of pro-inflammatory T helper subsets such as Th1 and Th17 cells, both of which are implicated in mediating neuroinflammatory damage in disorders like multiple sclerosis and neuromyelitis optica (Amoriello et al., 2024). Clinical evidence supports these immunomodulatory effects: selective serotonin reuptake inhibitors, commonly used antidepressants, have demonstrated a potential to reduce serum levels of IFN-γ and increase anti-inflammatory cytokines such as IL-10 in multiple sclerosis patients, suggesting that their therapeutic effects may extend beyond their neurological indications.

3.2 GABA-Mediated Suppression of Autoimmune Responses

GABA is the primary inhibitory neurotransmitter in the central nervous system, but it also plays a crucial role in immune regulation, particularly within the context of gut-brain-immune axis communication. Several gut-resident bacterial strains, including *Lactobacillus brevis, Bifidobacterium dentium*, and others, are known to synthesize GABA from glutamate via glutamate decarboxylase. Immune cells, including T lymphocytes and macrophages, express GABAA and GABAB receptors, allowing for direct interaction with microbiota-derived GABA (Zhang et al., 2022). Studies in autoimmune models have shown that GABA signaling can suppress T cell proliferation, inhibit pro-inflammatory cytokines such as IL-17 and IFN-γ, and enhance the differentiation of regulatory T cells (Tregs) (Bhandage et al., 2018). For example, in experimental autoimmune encephalomyelitis, a widely used mouse model of multiple sclerosis, oral administration of GABA led to reduced neuroinflammation, lower demyelination, and improved motor scores. GABA inhibitory effects extend to systemic autoimmunity as well, as seen in models of type 1 diabetes and rheumatoid arthritis. Clinically, multiple sclerosis patients exhibit decreased expression of GABA transporters on immune cells, suggesting a dysregulation of GABAergic signaling. Pharmacological agents such as ganaxolone, a GABAA receptor modulator, have shown promise in restoring immune homeostasis and reducing CNS inflammation (Paul et al., 2014). These findings highlight GABA central role in maintaining immune tolerance and its potential as a therapeutic target for autoimmune neurological disorders.

3.3 Dopamine's Dual Immunoregulatory Role

Dopamine, widely appreciated for its roles in reward, motivation, and motor function, is also produced peripherally and by gut microbiota, including species such as Escherichia coli, Bacillus spp., and Proteus mirabilis. Dopamine functions as an immunomodulatory molecule by acting on dopaminergic receptors expressed by T cells, B cells, dendritic cells, and macrophages (Feng and Lu, 2021). In the context of autoimmune neurological diseases, dopamine levels in the periphery have been inversely correlated with disease activity. For instance, during relapse phases in multiple sclerosis, dopamine levels are reduced, coinciding with elevated levels of Th17 cells and IL-17, both hallmarks of inflammatory pathology. Dopamine has been found to suppress IL-17 secretion from peripheral blood mononuclear cells, thereby modulating inflammatory responses. Additionally, dopamine impairs microglial activation, reducing nitric oxide production and chemotaxis, which can attenuate central inflammation (Wang et al., 2019). However, the effects of dopamine on the immune system are nuanced: depending on receptor subtype engagement, dopamine can exert both immunosuppressive and pro-inflammatory actions. Nonetheless, a relative depletion of dopamine, as observed in multiple sclerosis and Parkinson's disease, tends to favor a pro-inflammatory milieu. Strategies to enhance dopaminergic tone or modulate receptor-specific pathways may offer promising therapeutic directions in treating autoimmune neurological conditions.

3.4 Cholinergic Modulation of Gut and Systemic Immunity

The cholinergic system, particularly through the action of ACh, plays a pivotal role in maintaining immune equilibrium and gut barrier integrity. Unlike classical neuronal transmission, acetylcholine is also synthesized by non-neuronal sources, including epithelial cells of the gut and various immune cells such as T cells and macrophages. This non-neuronal cholinergic system contributes primarily mediated via the α7 nicotinic acetylcholine receptor (α7nAChR) (Beckmann and Lips, 2013). Activation of this receptor on immune cells leads to the suppression of pro-inflammatory cytokine release, including TNF-α, IL-1β, and IL-6, without affecting anti-inflammatory cytokines. Furthermore, acetylcholine signaling maintains gut epithelial integrity by modulating tight junction protein expression and preventing microbial translocation, which otherwise can trigger systemic immune activation. In autoimmune contexts, dysregulation of cholinergic signaling has been linked to exaggerated immune responses and barrier dysfunction. For example, in multiple sclerosis, altered expression of cholinergic enzymes and receptors has been observed in both peripheral blood and CNS-resident immune cells (Jiang et al., 2017). Moreover, vagus nerve stimulation has shown efficacy in reducing disease severity in autoimmune encephalomyelitis models and improving cognitive performance in neuroinflammatory conditions (Jin et al., 2023). Other gut-derived neurotransmitters such as norepinephrine and histamine also influence immune cell function; however, their roles in autoimmune neurological diseases are less well characterized. Nonetheless, emerging studies suggest these molecules may shape T cell polarization and influence CNS-targeted immune responses through microbiota-gut-brain interactions (Figure 1).

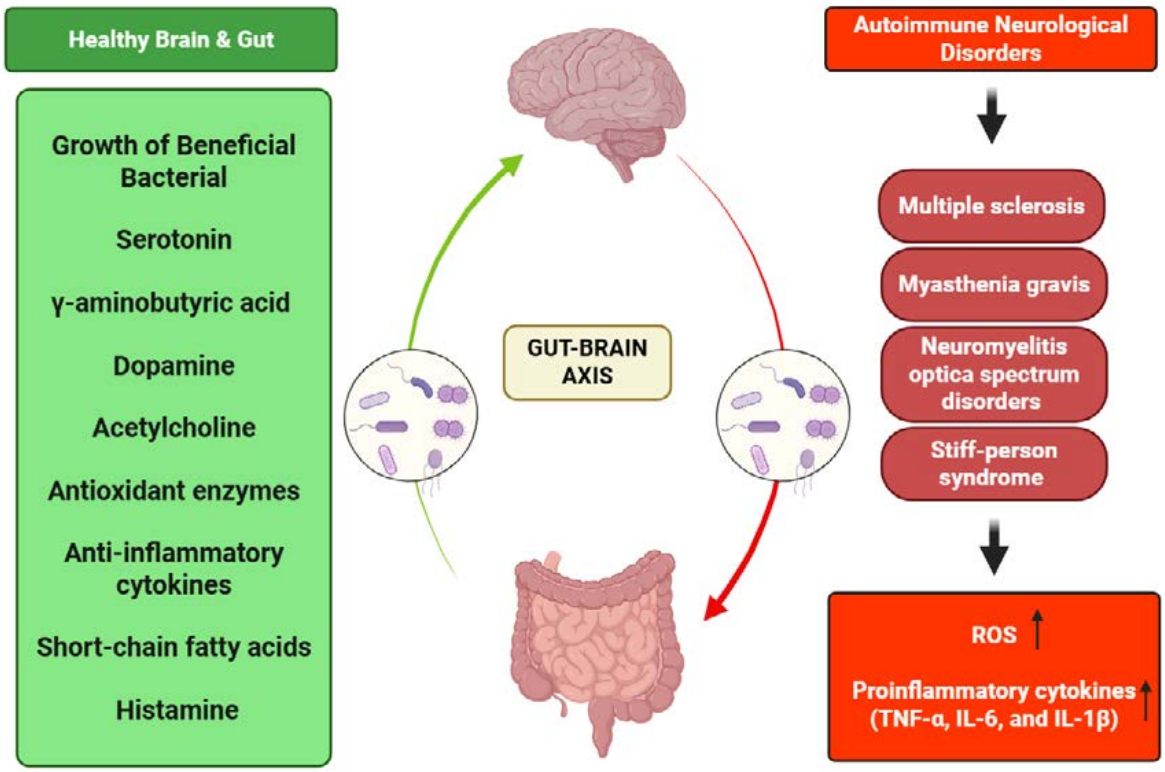

Figure 1: Comparative illustration of beneficial microbial metabolites (left) versus pathogenic drivers (right) in the gut-brain axis. Imbalances in gut-derived neurotransmitters and inflammatory signals are implicated in autoimmune neurological disorders.

4. Microbial Metabolites, Neurotransmitters, and Autoimmune Neuroinflammation

4.1 SCFAs

SCFAs are a group of microbial metabolites primarily composed of acetate, propionate, and butyrate, which are produced by the fermentation of indigestible dietary fibers by commensal gut microbiota. These molecules serve as key mediators of gut-brain-immune communication and have profound immunomodulatory effects relevant to the pathogenesis of autoimmune neurological disorders such as multiple sclerosis (Warren et al., 2024). In both preclinical and clinical studies, reduced levels of SCFAs have been reported in multiple sclerosis patients, correlating with disease activity and immune dysregulation. SCFAs modulate immune responses through several mechanisms: (i) they enhance the differentiation and stability of regulatory T cells by promoting histone acetylation through the inhibition of histone deacetylases (HDACs); (ii) they act as ligands for G protein-coupled receptors such as FFAR2 and FFAR3 (also known as GPR43 and GPR41), which are expressed on immune cells, thereby modulating immune signaling cascades; and (iii) they promote anti-inflammatory cytokine production, particularly IL-10. In experimental autoimmune encephalomyelitis, the mouse model of multiple sclerosis, supplementation with butyrate or propionate leads to a significant increase in Tregs and a concomitant reduction in pro-inflammatory Th1 and Th17 cells (Du et al., 2022), ameliorating clinical symptoms. Additionally, SCFAs directly influence CNS immune regulation by acting on microglial cells. Microglia, the resident immune cells of the CNS, require proper SCFA signaling via FFAR2 for their maturation and functional integrity. Deficiency in SCFAs leads to impaired microglial homeostasis and increased neuroinflammation (Caetano-Silva et al., 2023). Thus, SCFAs represent a critical bridge between gut microbial activity, neurotransmitter balance, and immune regulation in autoimmune neuroinflammatory diseases.

4.2 Bile Acids and Aryl Hydrocarbon Receptor (AHR) Ligands

Bile acids and AHR ligands represent another class of microbiome-derived metabolites that exert significant regulatory control over immune homeostasis and neuroinflammation. Bile acids, particularly secondary bile acids such as deoxycholic acid and lithocholic acid (LCA), are synthesized by gut microbes through enzymatic modifications of primary bile acids produced by the liver (Sarenac and Mikov, 2018). These secondary bile acids influence immune cell differentiation and cytokine production via the farnesoid X receptor and the Takeda G-protein-coupled receptor 5, which are expressed on dendritic cells, macrophages, and T cells. These receptors modulate the balance between pro-inflammatory and anti-inflammatory immune phenotypes. AHR activation in dendritic cells, T cells, and glial cells leads to increased IL-10 production, promotes Treg development, and inhibits Th17 differentiation (Prasad Singh et al., 2020), thereby restoring immune tolerance and suppressing autoimmune responses. In autoimmune encephalomyelitis models, pharmacologic or dietary enhancement of AHR ligand availability leads to disease attenuation, reduced CNS infiltration by inflammatory T cells, and improved neurological outcomes. Additionally, AHR signaling modulates microglial activity by shifting them from a pro-inflammatory phenotype to a neuroprotective one, further reinforcing the anti-neuroinflammatory potential of this pathway. Importantly, alterations in bile acid composition and reduced levels of AHR ligands have been observed in multiple sclerosis patients, supporting the translational relevance of these findings. Together, bile acids and AHR ligands exemplify how microbial metabolites orchestrate a complex network of immune and neurological interactions, influencing the susceptibility and progression of autoimmune neurological disorders.

5. Evidence in Specific Autoimmune Neurological Disorders

5.1 Multiple Sclerosis

Multiple Sclerosis is the best studied model linking gut neurotransmitters to autoimmunity. Patients display gut dysbiosis reduced SCFA producers (Faecalibacterium, Butyricimonas) and elevated proinflammatory taxa (Akkermansia, Clostridium perfringens). Altered 5-HT signaling due to microbiome changes and gut immune alterations leads to heightened Th17 pathways and disease activity (Kwon et al., 2019), while GABAergic deficits correlate with inflammatory flares. Dopamine deficiency increases IL-17, and dysregulated bile acids impair AHR-mediated tolerance. SCFA supplementation and microbiome interventions show promise in reducing relapse and neuroinflammation in human and animal studies

5.2 Stiff-Person Syndrome

SPS is characterized by glutamate decarboxylase autoantibodies and impaired GABA signaling in motor neurons (Dalakas, 2022). Although direct gut neurotransmitter links are yet unexplored, dysregulated GABA metabolism and autoantibody production suggest GABA-producing gut microbes may influence disease onset or severity. GABA deficits contribute to hyperexcitability and immune dysregulation in SPS.

6. Future Perspectives

The interplay between gut-derived neurotransmitters and microbial metabolites offers promising avenues for the development of innovative therapeutic strategies in autoimmune neuroinflammation, such as multiple sclerosis. Probiotic therapy represents a key frontier, with specific strains like Lactobacillus brevis, Bifidobacterium dentium, and Bacteroides fragilis showing potential to modulate neurotransmitter levels, including GABA and serotonin, and enhance the production of immunoregulatory short-chain fatty acids. These probiotics could help rebalance gut-brain-immune signaling and suppress pro-inflammatory pathways.

Dietary interventions also play a critical role. Increasing intake of microbiota-accessible carbohydrates boosts SCFA production, which in turn promotes regulatory T cell differentiation and suppresses Th17 responses. Similarly, diets enriched in tryptophan can stimulate the

generation of serotonin and AHR ligands such as indoles and kynurenines, supporting immune tolerance and reducing neuroinflammation. Pharmacological strategies already in use such as selective serotonin reuptake inhibitors may exert additional immunomodulatory effects beyond mood regulation by influencing cytokine production. Novel agents targeting GABAergic and dopaminergic pathways also show promise in preclinical models. Additionally, gut-derived biomarkers such as SCFAs, bile acids, and neurotransmitter levels could be developed to monitor disease progression and therapeutic response. Finally, future research using germ-free or gnotobiotic animal models will be instrumental in defining causality and guiding the design of precision microbiota-based treatments. These multidisciplinary approaches could revolutionize how we diagnose, monitor, and treat neuroimmune disorders through the gut-brain-immune axis.

7. Conclusion

Gut-derived neurotransmitters including serotonin, GABA, dopamine, and acetylcholine serve as key mediators at the nexus of the microbiota gut brain immune interface. They influence immune cell function, CNS neuroinflammation, and autoimmune responses. Dysbiosis-induced imbalances in neurotransmitter levels and signaling can exacerbate autoimmune neurological disorders, particularly multiple sclerosis. Interventions targeting microbial producers, dietary intake, or receptor signaling may offer novel strategies for prevention and therapy. A comprehensive understanding of these complex pathways promises to transform future approaches to the treatment of neuroimmune disorders.

Declarations

Ethics approval statement

Not applicable

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

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During the preparation of this work the authors used AI-assisted technology QuillBot, in order to check the grammar and spell in some sentences

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