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Understanding the Gut-Brain Connection: Exploring Its Impact on Neurological Health, Neurodegenerative Diseases, and Depression

ნაწლავ-ტვინის კავშირის გაგება: მისი გავლენის შესწავლა ნევროლოგიურ ჯანმრთელობაზე, ნეიროდეგენერაციულ დაავადებებზე და დეპრესიაზე

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Abstract

Introduction: The microbiota gut-brain axis or the (MGBA) that incorporates gut microbiota (GM) is known to control the defensive system of our body along with the well-being of the central nervous system (CNS). The GM represents parasitic microorganisms that if in abnormal ratios throughout the body, may result in exposure to diseases, for example, Alzheimer's and Parkinson's. This research aims to clarify the molecular pathways through which GM dysbiosis impacts neurological health and will explore the effectiveness of probiotics and Synbiotics in restoring GM balance to improve brain function. **Methodology:** A comprehensive literature review was conducted, analysing peer-reviewed studies on the microbiome studies, the implications of probiotics, Synbiotics, and changes in nutrition on the composition of GM and the neuroinflammatory response of an organism. **Results:** The data indicate that these approaches assist in the re-establishment of adequate diversity in the GM population which helps to reduce the extent of neuroinflammation, stabilize the functioning of neurotransmitter deregulation, and enhance cognitive performance. The findings indicate the critical potential of biological agents targeting gut microbiota in the treatment of some neurological conditions. **Conclusion:** the modulating of GM represents a new understanding and mechanisms that can help deal with issues associated with brain health and manage prevalent complications of neurodegenerative diseases while reiterating the need for microbiome balance for the optimal functioning of CNS.

Keywords: Microbiota gut-brain axis, dysbiosis, short chain fatty acids, gut microbiota, microbiota-derived metabolites, neurodegenerative diseases, probiotics and prebiotics, depression, Fecal microbiota transplantation

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აბსტრაქტი

შესავალი: მიკრობიოტა ნაწლავ-ტვინის ღერძი, რომელიც აერთიანებს ნაწლავის მიკროფლორას (GM), აკონტროლებს ჩვენი სხეულის დაცვით მექანიზმებს და უზრუნველყოფს ცენტრალური ნერვული სისტემის (ცნს) ჯანსაღ ფუნქციონირებას. ნაწლავის მიკროფლორა (მიკრობიოტა, მიკრობიომი) წარმოადგენს პარაზიტულ მიკროორგანიზმებს, რომლებმაც არანორმალური თანაფარდობის შემთხვევაში შეიძლება გამოიწვიონ რიგი დაავადებები, მაგალითად, ალცჰეიმერის და პარკინსონის დაავადება. კვლევა მიზნად ისახავს მიკრობების და მათი მეტაბოლიტების, განსაკუთრებით მოკლე ჯაჭვის ცხიმოვანი მჟავები (SCFA) როლს ცნს-ის ჯანმრთელობის შენარჩუნებაში. **მეთოდოლოგია:** დამუშავდა და გაანალიზდა შესაბამისი ლიტერატურიდან მოძიებული თეორიული მასალა. **შედეგები:** მონაცემები მიუთითებს, რომ ეს მიდგომები ხელს უწყობს ნაწლავის მიკროფლორის პოპულაციის ადექვატური მრავალფეროვნების აღდგენას, რაც ხელს უწყობს ნეიროანთების მასშტაბის შემცირებას, ნეიროტრანსმიტერების დერეგულაციის ფუნქციონირების სტაბილიზაციას და კოგნიტური ეფექტურობის გაზრდას. დასკვნები მიუთითებს ბიოლოგიური აგენტების კრიტიკულ პოტენციალზე, რომლებიც მიზნად ისახავს ნაწლავის მიკროფლორის რეგულირების პოტენციალის შესწავლას ზოგიერთი ნევროლოგიური მდგომარეობის მკურნალობაში. **დასკვნა:** ნაწლავის მიკროფლორის მოდულაცია წარმოადგენს ახალ გაგებას და მექანიზმებს, რომლებიც დაგვეხმარება გავუმკლავდეთ ტვინის ჯანმრთელობასთან დაკავშირებულ საკითხებს და ვმართოთ ნეიროდეგენერაციული დაავადებების გავრცელებული გართულებები, ამასთან, მყარად უნდა გვახსოვდეს ნაწლავის მიკროფლორის ბალანსის აუცილებლობა ცნს-ის ოპტიმალური ფუნქციონირებისთვის.

საკვანძო სიტყვები: ნაწლავის მიკროფლორა (ნაწლავის მიკრობიოტა), ნაწლავ-ტვინის ღერძი, დისბიოზი, მოკლე ჯაჭვის ცხიმოვანი მჟავები, მიკრობიოტასგან მიღებული მეტაბოლიტები, ნეიროდეგენერაციული დაავადებები, პრობიოტიკები და პრებიოტიკები, დეპრესია, ფეკალური მიკრობიოტის ტრანსპლანტაცია.

ციტატა: ახილ კრიშნან ვიკრამან პილაი. ნაწლავ-ტვინის კავშირის გაგება: მისი გავლენის შესწავლა ნევროლოგიურ ჯანმრთელობაზე, ნეიროდეგენერაციულ დაავადებებზე და დეპრესიაზე. ჯანდაცვის პოლიტიკა, ეკონომიკა და სოციოლოგია, 2025; 9 (1). https://doi.org/10.52340/healthecosoc.2025.09.01.02.

Introduction

The gut microbiota (GM) is an indispensable component that directs the host physiology and the host's defense system alongside the central nervous system (CNS) by the gut-brain axis (MGBA). Broadly, the microflora in our gastrointestinal (GI) system contains many phyla, including but not limited to, Bacteroidetes, Firmicutes, Proteobacteria, and Actinobacteria as well as smaller groups comprising verrucomicrobia and fusobacteria. These microbial communities are an important part of the microbiota gut-brain axis or the (MGBA) that involves a large interaction of the GI system and the CNS. The communication within MGBA, in turn, is characterized by two-way or bilateral actions and is a huge interface along neural, immune, as well as hormonal systems which include the vagus nerve, hypothalamic–pituitary–adrenal (HPA) axis, short-chain fatty acids (SCFAs) and each plays an indispensable part in the maintenance of the gut homeostasis and functionality of the CNS. Periodically dysbiosis of the GM, that is imbalance of the GM, has been found to pave the way to several neurological disorders, including Parkinson's disease (PD), Alzheimer's disease (AD) as well as depression.

While evidence advocates a link between dysbiosis and neurodegenerative disorders, the precise molecular mechanisms underlying these associations are not well defined. This research seeks to identify how dysbiosis contributes to neurological disorders, focusing on the involvement of microbial metabolites, neuroinflammation, and neurodegeneration in these processes. The study also aims to explore potential interventions, such as probiotics and Synbiotics, to restore GM balance and potentially mitigate the effects of these disorders.

Investigating the role of GM in CNS functions is essential for advancing the understanding of microbiology and neuroscience. This research could provide a new framework for understanding the pathogenesis of neurological diseases.

The rising prevalence of neurodegenerative and psychiatric diseases underscores the urgent need for effective treatments. This research may provide therapeutic strategies that target GM modulation to help improve clinical outcomes for individuals with these conditions.

Understanding how to regulate GM to lift the burden of neurological diseases can reduce healthcare costs and raise living standards for a large population segment.

Studies highlight the considerable influence GM has on brain health, particularly through metabolites mainly involving short-chain fatty acids (SCFAs) and neuroactive components synthesized in our GI system. by the microflora. The MGBA has now sprouted as a new topic of interest in microbiology and neuroscience. Several studies suggest changes in the configuration of the gut microbes are interconnected to several neurological conditions, including Parkinson's, Alzheimer's, and mood disorders. These conditions may be exacerbated by inflammation and neurodegeneration. Some studies scouted the potential of implementing probiotics, Synbiotics, and dietary interventions to regain the GM and narrow down symptoms of neurological disorders, suggesting a promising area for further exploration. Despite the growing body of evidence linking GM to brain function, the detailed mechanisms through which GM influences neuroinflammation and neurodegeneration remain insufficiently understood.

This research aims to clarify the molecular pathways through which GM dysbiosis impacts neurological health and will explore the effectiveness of probiotics and Synbiotics in restoring GM balance to improve brain function.

Methodology

A literature search was conducted in electronic databases such as PubMed, Google Scholar, and EBSCO using appreciate, keywords such as microbiota gut-brain axis, MGBA, dysbiosis, short chain fatty acids, SCFA, gut microbiota, microbiota-derived metabolites, neurodegenerative diseases, probiotics and prebiotics, depression, Fecal microbiota transplantation.

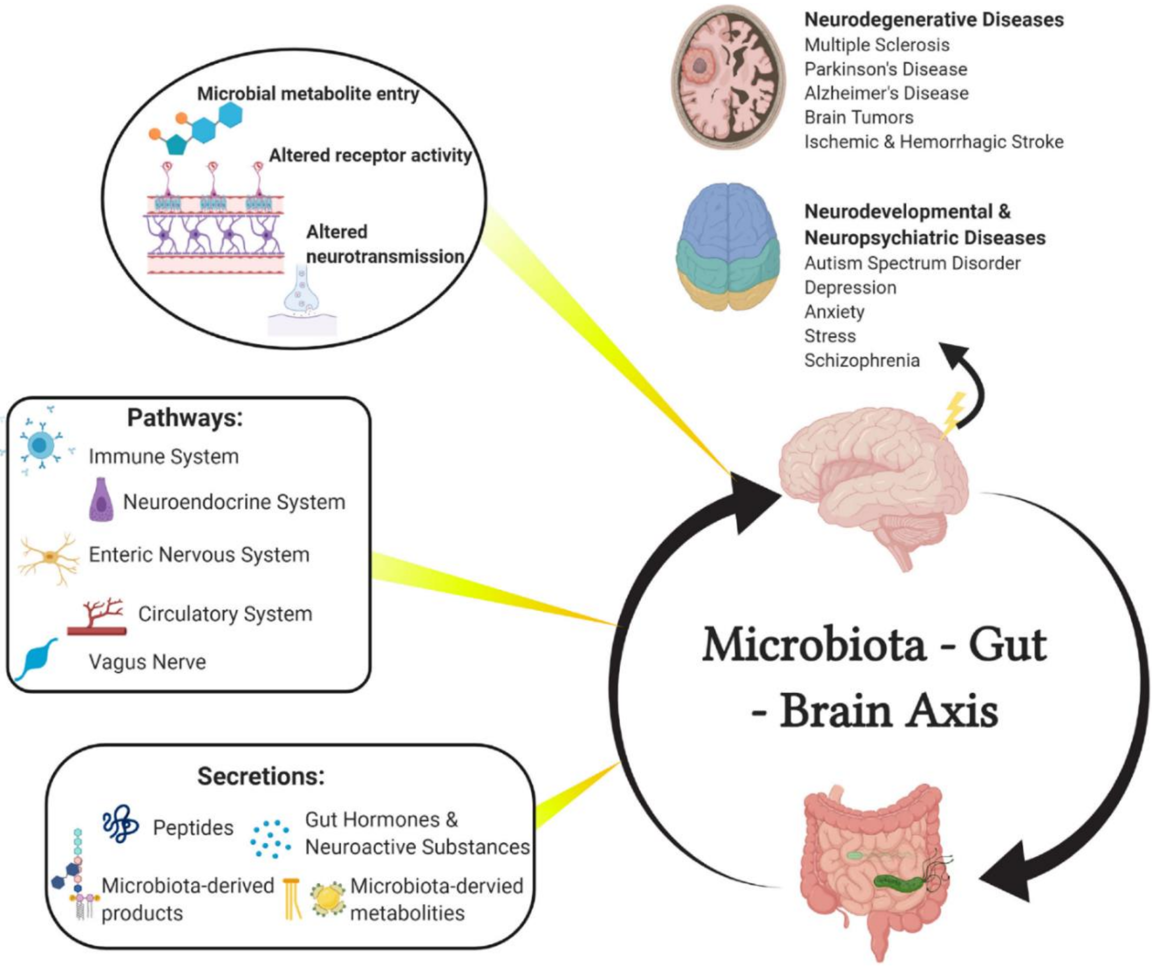
Literature review

The gut-brain axis (GBA) connects the GI system with the CNS using neurological, endocrine, and immune pathways via mutual interaction. This communication has an indispensable function in maintaining physiological and neurological homeostasis. The gut microflora involves a huge variety of microorganisms that occupy the GI tract and has been found to have a major influence over the interaction between the GI system and the CNS. By synthesizing several neurotransmitters and metabolites, and by immune modulation, the gut microflora has a significant influence on cognitive, emotional, and overall neurological health.

Neural Communication: Role of the Vagus Nerve

The Vagus nerve is an essential element linking the gut-brain axis that bridges our gastrointestinal system and the central nervous system via nerve signaling. This helps in regulating multiple GI functions, including GI motility, GI secretion as well as permeability. Vagal activity is sensitive to stress, which can alter signaling pathways, resulting in GI dysfunction, and influencing the function of the brain (Han et al 2022). The gut microflora orchestrates the synthesis of neurotransmitters, namely GABA), dopamine and serotonin, associated with mood, behavior, and cognitive functions of the human mind. These neurotransmitters emphasize the gut's significant role in maintaining CNS health and regulating psychological and neurological processes (Chen et al., 2021).

Figure 1: The microbiota-gut-brain axis



The Endocrine Pathways via Hypothalamic-Pituitary-Adrenal (HPA) Axis

The HPA shoulders a decisive role in how the body responds to stress and modulates gut-brain communication. When under stress, the hypothalamus starts to release corticotropin-releasing hormone (CRH), which triggers the pituitary gland to give out adrenocorticotropic hormone (ACTH), prompting the adrenal gland to produce cortisol from the adrenal cortex. Chronic stress, and subsequent elevated cortisol levels, can disrupt the gut microbiota composition, promoting dysbiosis. Dysbiosis is a condition where the imbalance or variation in the gut microflora exacerbates neuroinflammation, contributing to cognitive dysfunction and developing several psychiatric conditions including anxiety and depression (Ahmed et al. 2024). Thus, the HPA axis links stress with microbiota-mediated brain health, demonstrating the crucial interplay between endocrine signaling and neuroinflammation.

Immune Pathways and Cytokine Signaling of the Gut-Brain Axis

Our body's defense system, which is the immune system, contributes its part in the working of the gut-brain axis, especially in regulating neuroinflammation. It has been found that Pro-inflammatory cytokines, namely interleukin-6 (IL-6) as well as tumor necrosis factor-alpha (TNF-α), are permeable to the BBB and therefore induce inflammation of the CNS and initiate the development of degenerative diseases of the CNS namely AD and PD. So, the gut microflora is significant for immune modulation, resulting in the production of cytokines and thereby impacting brain health. Dysbiosis disrupts this equilibrium of the gut flora, leading to systemic inflammation that increases the risk of developing neurological disorders (Kandpal et al., 2022).

Gut Microbiota and Neuroactive Metabolites

The gut microflora is significant in the synthesis of bioactive metabolites namely, short-chain fatty acids (SCFAs)—acetate, propionate, and also butyrate, by utilizing dietary fibers by fermenting them. These SCFAs can influence brain health by regulating the neuroinflammatory responses while trying to maintain the integrity of the BBB and the supply of energy to the cells present in our CNS. Butyrate is found to have an anti-inflammatory effect as well as defend the brain from being prone to neurodegenerative damage (Silva et al. 2020). Dysbiosis can alter SCFA production which may cause an increase in intestinal permeability as well as inflammation leading to chronic low-grade inflammation, which collaborates with diseases namely AD and PD. Therefore, SCFAs are essential for linking the gut microflora with brain health, illuminating the necessity for a microbial balance for neuroprotection.

Role of Neurotransmitter and the Gut Microflora

Gut microflora has a noticeable influence over regulating numerous neurotransmitters that are engaged in mood, cognition, as well as behavior. These neurotransmitters, namely acetylcholine (Ach), serotonin, GABA, and norepinephrine, are synthesized and or regulated by gut microflora using various mechanisms.

Acetylcholine (Ach)

Acetylcholine (Ach) plays a cardinal role in cognitive functions including learning and memory, and in facilitating excitatory signal transmission between neurons in the CNS and PNS. Any disturbance in the regulation of Ach is related to neurodegenerative diseases like Alzheimer's disease. Initially, it was linked to acetylcholine produced by Bacillus, but now it has been discovered that various bacteria in our GI tract, namely Bacillus subtilis, Escherichia coli, Lactobacillus plantarum, and Staphylococcus aureus, also synthesize Ach, where B. subtilis produces the highest amount. Probiotics, namely Lactobacillus species, are capable of enhancing Ach production, potentially improving cognitive function, and reducing memory deficits associated with neurodegenerative diseases (Ojha et al., 2023). Although Ach is restricted by the BBB, it is synthesized in the brain using choline and acetyl coenzyme A. Choline, which is obtained from peripheral sources, is then transported to the brain using capillary endothelial cell carriers.

Serotonin (5-HT)

Serotonin is primarily synthesized in the brain's raphe nuclei, and it regulates several functions including our mood, sleep, and cognition. Disruption in serotonin function is linked to the development of psychotic disorders like anxiety and depression. Interestingly, 90% of the serotonin is synthesized peripherally, by the enterochromaffin cells of the GI system. Albeit serotonin cannot cross the BBB, its precursor, tryptophan, can. Amidst the gut microflora, Clostridia is found to enhance serotonin production by over-expression of tryptophan hydroxylase 1 (TPH1) in enterochromaffin cells. Elevated peripheral serotonin levels can influence central nervous system function by enhancing the permeability of the BBB, thus impacting mood and cognition.

Gamma-Aminobutyric Acid / (GABA)

The GABA is a neurotransmitter serving inhibitory function and is synthesized in the brain from glutamate by GABAergic neurons. Interestingly, gut microflora, which includes Bacteroides fragilis, Bifidobacterium, Parabacteroides, and Eubacterium, is also found to produce GABA. While GABA cannot cross the BBB, it may interact with the enteric nervous system or via the vagus nerve. Also, metabolites like acetate, synthesized by gut bacteria by the process of fermentation, can cross the BBB and influence GABA metabolism in the brain, especially in the hypothalamus. Dysbiosis in GABA-producing microbes is associated with mood changes, such as anxiety and depression. GABA's effects on the brain are mediated through vagal signaling, influencing emotional regulation.

Norepinephrine (NE)

Norepinephrine (NE) is a catecholamine neurotransmitter that plays a fundamental role in the CNS and PNS, that regulates processes like arousal, attention, memory, and the acute stress response (fight-or-flight). In our brain, NE is chiefly synthesized in the locus coeruleus, where tyrosine is converted to dopamine, and this dopamine is the precursor of norepinephrine, leading to its synthesis. Recent evidence suggests that gut microflora influences NE synthesis, with environmental factors, such as temperature, modulating microbial composition. These changes can affect NE release in peripheral tissues, which also includes the intestine and brown adipose tissue, that contributes to the regulation of heat and energy by providing thermoregulation, particularly in response to cold exposure. Furthermore, dysregulation of NE synthesis, potentially driven by alterations in the gut microbiome, has been interlinked with neuropsychiatric disorders namely schizophrenia and Parkinson's disease (Holland et al., 2021).

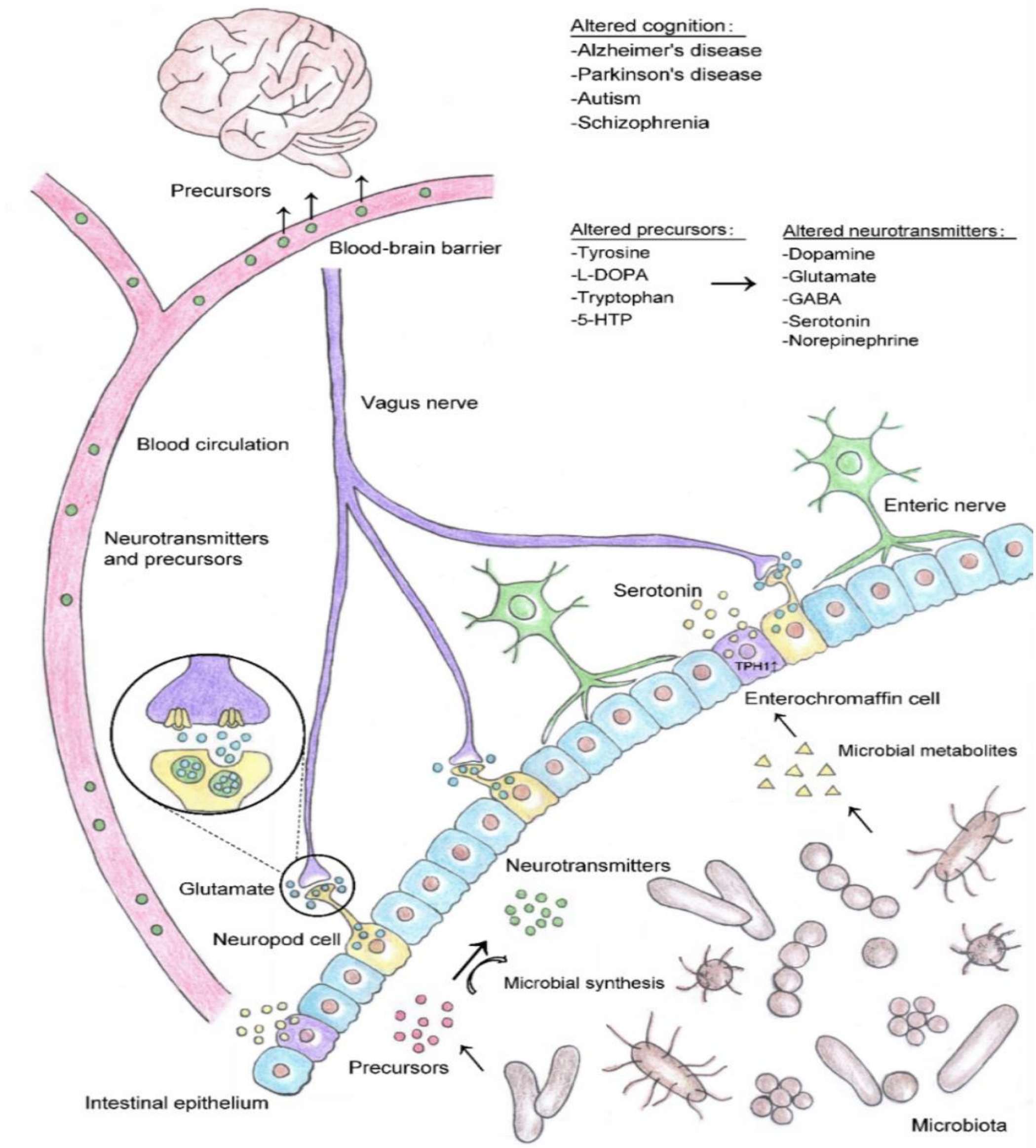


Figure 2: Gut Microflora and Its Influence on Synthesizing neurotransmitters and its impact on Cognitive Function (Chen et al., 2021)

Dietary Influence on Gut Microbiota and CNS Health

Our diet plays an elemental part in organizing the gut microflora composition, which influences brain health. Diets rich in fiber contribute to the proliferation of useful microbes, namely Lactobacillus and Bifidobacterium, which help in the synthesis of SCFAs that support cognitive function and immune balance, while on the other hand, diets rich in refined sugars and unhealthy fats promote dysbiosis, which has been associated with neuroinflammation and decline in cognitive function (Maia et al., 2024). Therefore, dietary patterns significantly impact the gut-brain axis and brain health.

Therapeutic Potential of Gut Microbiota Modulation

Modulating gut microflora composition offers a promising strategy for treating neurological disorders. Probiotics, prebiotics, and dietary interventions can restore ambient microflora that balances and reduces inflammation, thereby improving cognitive function in preclinical models. For example, probiotics can reduce amyloid-beta deposition thereby improving cognitive functions in patients with Alzheimer's disease. Individualized nutrition, plans based on the person's specific microflora, can optimize brain health, and treat conditions notably, anxiety, depression, and other neurodegenerative diseases.

Discussion

GBA has now turned out to be an elemental system that connects the GI system and the CNS. Multiple studies conducted to date suggest that gut microflora has a profound influence on brain health and contributes to the pathogenesis of CNS pathology, including AD, PD, depression as well as anxiety, and mood disorders. Dysbiosis, or microbial imbalance in the gut, disrupts these pathways that connect the brain and the GI system, which hinders brain function and the progression of these diseases.

Mechanisms by which GM Dysbiosis Drives Neurological Disorders

Dysbiosis contributes to neurological disorders through several pathways. One primary mechanism is immune system dysregulation. The gut microflora influences systemic inflammation, which is involved in several neurodegenerative diseases. When the gut microflora is imbalanced, it results in increased intestinal permeability, often known as "leaky gut." A barrier that is compromised makes endotoxins permeable to lipopolysaccharides (LPS) that then trespass into the systemic circulation, activate the immune system, and thereby lead to neuroinflammation. Studies show that LPS is capable of triggering neuroinflammatory responses that can exacerbate diseases such as AD and PD (Kalyan et al., 2022).

Another key mechanism involves mainly neurotransmitter regulation. The gut microflora is relevant for synthesizing neurotransmitters namely serotonin, dopamine, and GABA, where all of which play an indispensable role in regulating mood, cognition, and behavior. Dysbiosis may gradually result in an imbalance in these neurotransmitters, contributing to mood disorders, cognitive decline, and even neurodegenerative diseases. For example, a decline in the synthesis of serotonin that was caused due to disruption in microflora is linked to anxiety and depression.

Moreover, the metabolites that are synthesized by the gut microflora, especially SCFAs such as butyrate, propionate, and acetate, are found to have an essential function in modulating brain health. These metabolites can influence the integrity of the BBB, enhancing neurogenesis, and can reduce neuroinflammation. Butyrate, for example, has been shown to protect against any cognitive decline mainly by preventing BBB leakage, and therefore reducing neuroinflammation, which is crucial for diseases such as Alzheimer's and Parkinson's. Dysbiosis alters the production of such beneficial metabolites that gradually leads to the weakening of the defense mechanisms of the brain and therefore contributes to neurodegeneration.

Role of Microbial Metabolites for CNS Health and Neuroinflammation

Microbial metabolites, namely SCFAs and other bioactive components have a profound influence on CNS health and neuroinflammation. SCFAs are synthesized in the GI tract when gut microflora ferments dietary fibers. It is shown to exert great anti-inflammatory influence on the brain. Butyrate is found to possess neuroprotective properties. It contributes to the maintenance of the BBB and therefore prevents the entry of these substances into the brain, preventing stimulation of inflammation of neurons and also preventing nerve damage. This mechanism is elementary in the context of AD, in which the impaired BBB integrity is the main hallmark for the progression of neurological diseases.

SCFA can also regulate the immune responses by reducing the activation of microglia that occupy the brain whose function is immunity. This reduction in the activation of microglia can alleviate neuroinflammation, which is a significant factor that contributes to the development of degenerative diseases of the CNS like Parkinson's (Isik, 2023). Furthermore, these metabolites can enhance neuronal health by assisting in neurogenesis, thereby providing a great contribution to cognitive resilience as well as protection against aging-related neurodegenerative diseases.

Therapeutic approach using Probiotics, Synbiotics, and Dietary Interventions

Multiple therapeutic trials are done to regain the gut microflora balance as well as improve neurological outcomes, especially in patients affected with neurodegenerative diseases. Probiotics which are rich in favorable live microorganisms and Synbiotics, which is a combination of probiotics and prebiotics seem to provide novel therapeutic possibilities. Multiple studies have proven that probiotics can alleviate neuroinflammation and by doing so, it can improve the cognitive function in cases of AD (Anderson, 2022). These beneficial bacteria have the potential to restore gut microbial diversity, adjust immune responses, and even enhance the synthesis of neuroactive compounds, such as SCFAs and neurotransmitters.

Dietary interventions also maintain a significant duty in modulating the gut microflora. Food that is rich in fiber, polyphenols, and omega-3 fatty acids can supplement the gut microflora diversity and assist in the production of SCFA. For example, a Mediterranean diet which involves the consumption of food such as fruits, vegetables, and good fats that are beneficial for the body is found to have a mandatory role in reducing the risks of neurodegenerative diseases as well as in improving cognitive function. On the other hand, diets rich in refined sugars and unhealthy fats, mainly saturated fats and processed foods promote microbial imbalances that increase the risk of neuroinflammation and neurodegeneration and even alter the GI system functions.

Fecal microbiota transplantation (FMT) is a novel therapeutic strategy that has proved to possess the potential to restore the gut microflora balance. Clinical studies in PD models have shown that FMT can decrease motor symptoms and reduce inflammation of the nervous system (Sadowski et al. 2024). FMT has been proven to restore healthy microflora that enhances the synthesis of SCFAs and therefore improves gut-brain signaling which may result in better neurological outcomes in those patients suffering from PD, AD, and other neurodegenerative diseases.

Conclusion and recommendations

The gut-brain axis possesses a significant function in the initiation as well as the aggravation of disorders related to the CNS. Dysbiosis in the GI tract acts as a critical component in the disruption of brain function. Disruptions in gut microflora composition can result in a hyperactive immune response that may trigger neuroinflammation, making it an epicenter of the pathogenesis of neurological diseases such as AD, PD that mainly result in neurodegeneration or other neuropsychiatric disorders namely anxiety, depression, and mood disorders. Moreover, dysbiosis is closely linked with imbalances in neurotransmitter regulation that can impact mood and cognitive processes.

Microbial metabolites, especially SCFAs, are elemental in balancing CNS health by regulating inflammation of the nervous system and preserving the blood-brain barrier integrity. They are chiefly produced by the fermentation of dietary fibers in our GI system that serve as signals that modulate the immune system and influence neuroinflammatory responses. Their deficiency may pave the way for the development of neurodegeneration and associated symptoms. Moreover, other bioactive components that are synthesized by gut microflora are found to have a direct impact on brain function by interacting with the neural pathways, further highlighting the necessity for a well-balanced microflora in our GI system.

Therapeutic methods mainly prioritize restoring the gut microflora balance, by including probiotics, Synbiotics, and dietary interventions in the daily diet. FMT has been shown to have a promising effect in mitigating the effects of dysbiosis. These approaches mainly work by enhancing the level of microbial diversity and therefore reducing systemic inflammation and improving our cognitive functions. Several interventions have been introduced because of numerous research that can modify the gut microflora and finally lead to improvements in neurological symptoms, offering a potential complementary strategy for treating neurodegenerative diseases. Thus, maintaining a healthy gut microflora through these therapeutic approaches presents an exciting avenue for improving CNS health and combating neurological disorders.

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