GUT–Brain Axis Modulation Through Prebiotic and Probiotic Botanicals

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***Abstract* -- Gamma-aminobutyric acid (GABA) is one of the most important inhibitory neurotransmitters in the human brain. It plays a central role in maintaining the balance between neuronal excitation and inhibition, thereby influencing mood regulation, emotional stability, and stress response. In recent years, scientists have discovered that GABA's function is not restricted to the brain alone but also extends to the gut, where it forms part of a complex bidirectional communication system known as the gut–brain axis. This system links the central nervous system (CNS) with the gastrointestinal tract, allowing signals to travel in both directions. Growing evidence suggests that the gut microbiota – the diverse community of microorganisms living in the intestines – contributes significantly to this communication through what is called GABAergic signaling. Certain gut bacteria are capable of producing GABA or modulating its receptors, thereby directly influencing neural pathways that regulate stress, anxiety, and even cognitive functions. This emerging field of research, often referred to as the microbiota–gut–brain axis, is shedding light on how mental health can be shaped by gut health. Probiotics and prebiotics have become important focus areas in this context. Probiotics are live microorganisms that, when consumed in adequate amounts, confer health benefits to the host. Some strains, such as *Lactobacillus rhamnosus* and *Bifidobacterium longum*, have demonstrated the ability to either produce GABA or positively influence its signaling pathways. In animal studies, these bacteria have been linked to reduced anxiety-like behavior, suggesting that they may act as natural modulators of mood. On the other hand, prebiotics – dietary fibers that serve as nourishment for beneficial gut bacteria – also play a crucial role. By encouraging the growth and activity of probiotic strains, prebiotics indirectly enhance the production and activity of GABA. This dual approach of combining probiotics with prebiotics, often referred to as synbiotics, is now being explored as a promising natural strategy for mental health support.**

Altogether, these findings highlight the therapeutic potential of microbiota-based interventions. By targeting GABA regulation through gut bacteria, it may be possible to develop novel, nonpharmacological approaches for managing conditions such as anxiety, depression, and stress-related disorders. This perspective represents an exciting shift in neuroscience and mental health research, emphasizing the power of nutrition and microbial balance in shaping brain function and emotional wellbeing.

***Index Terms*- Gut-brain axis, prebiotics, probiotics, psycobiotics, mental health.**

INTRODUCTION

It's a bilateral communication system that interconnect the central nervous system (CNS) to the gastrointestinal tract. There is more evidence that the brain axis connects gut bacteria by GABAergic signalling.[1] It is now well acknowledged that the organisms of the gastrointestinal system have an important function in mood, cognition, psychopathology, and other aspects of health and illness. However, there is still much work to be done before we fully understand the possible mechanisms causing this link complexity.[2] Novel medications have focused their sights to the gut microbiome with the goal of altering gut microbial metabolism for the improvement of energy balance, host immunity, and mental health. As a means of influencing the host microbiota and as a possible treatment for mood disorders, such as major depressive disorder (MDD), prebiotics and probiotics have emerged as a key component of research on the microbiota–gut–brain axis.[3] Certain probiotic strains, such as *Lactobacillus rhamnosus* and *Bifidobacterium longum*, have shown promising results in animal studies, either producing GABA or interacting with its receptors to help reduce anxiety-like behaviours.[4] However, due to limited sample sizes, brief trial durations, and a variety of trial designs, most of human clinical studies provide inconsistent results,[1] which has increased interest in psychobiotics, which are treatments intended to enhance mental wellness through gut regulation.[5]

1. HUMAN MICROBIOME

All of the microbial species and their associated genetic material found in the human body are

collectively referred to as the microbiome. All of the microorganisms in a specific area, such the skin or GI tract, are referred to as the microbiota.[6] The best way to characterise the microbiome of humans is as "the sum of all the microbes living within or around the human organism."[7] From birth up until death, the microbiome in a healthy host adapts and changes continuously to keep its immune system in a homeostatic balance. After birth, the microbiome of humans keeps evolving under the influence of external variables including food, medical treatment, exposure to toxins and diseases, as well as host factors like the immune systems that are both innate and adaptive.[8] Firmicutes and Bacteroidetes are the two most prevalent species of bacteria in the human gut, via Actinobacteria, Proteobacteria, and Verrucomicrobia following immediately after. Age, genetics, mode of birth, nutrition, stress, and antibiotic usage are only a few of the elements that may substantially alter the microbial composition.[9]

2. PREBIOTICS

Prebiotics are indigestible substances that particularly activate bacteria that are beneficial in the gut. Prebiotics provide beneficial bacteria, particularly Bifidobacteria and Lactobacilli, with "food" that promotes their growth and enhances gut health.[10]

Inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS) are common prebiotics that are found naturally in foods including chicory root, garlic, onions, and bananas. After being eaten, they undergo the fermentation by gut bacteria, which results in the production of short-chain fatty acids (SCFAs) like butyrate, which are good for the gut lining and may have an impact on brain function.[11] Prebiotics have been shown in recent studies to boost immune system modulation techniques, lower stress and anxiety, and enhance sleep quality in addition to supporting digestive health. Since the gut-brain axis is thought to be the mechanism leading these mental health benefits, prebiotics may be psychobiotics.[12]

3. PROBIOTICS

Probiotics are live microorganisms that, when given in adequate amounts, help the host's health, particularly by improving or reestablishing gut flora. These microorganisms, which are present in fermented items like yoghurt, and supplements, are most frequently strains of Lactobacillus, Bifidobacterium, and Saccharomyces boulardii.[13] Probiotics decrease harmful microbes, strengthen the intestinal barrier, control immune function responses, and modify the gut microbiota. In addition to improving gut health, they can also affect the gut–brain axis by lowering inflammation and generating neurotransmitters (including serotonin and GABA), which are crucial for mood, mental health, and cognition.[6],[14]

From recent studies, probiotic strains have been found to reduce the symptoms of stress, anxiety, and depression that is “psychobiotics”. However, strain-specific activity is significant because not all probiotics have an equal impact. Although encouraging, clinical data is still developing.[15]

4. MICROBES

Research has progressively identified specific probiotic strains as psychobiotics with potential advantages for brain health. For example, it has been demonstrated that Lactobacillus casei Shirota elevates mood and lessens feelings of anxiety in those who are depressed.[16] In patients with mild cognitive impairment, Bifidobacterium breve A1, another wellresearched strain, has shown cognitive advantages via enhancing remembering and lowering inflammation.[17]

5. KEY MICROBIAL PLAYERS IN THE GUT-BRAIN AXIS

Although there is a large variety of microorganisms in the gut, some species are particularly recognised for their capacity to affect brain function. Lactobacillus and Bifidobacterium are two of the most widely studied beneficial groups. It has been demonstrated that these bacteria lower inflammation, enhance mood and cognition, and alter neurotransmitter levels like GABA and serotonin.[18] Other significant components include Akkermansia muciniphila, which maintains the integrity of the gut barrier, and Faecalibacterium prausnitzii, which has anti-inflammatory qualities. An imbalance in these important bacteria, known as dysbiosis, has been connected to neurodevelopmental disorders like autism, anxiety, and depression.[19] Every one of these microorganisms makes a distinct contribution to gut-brain communication. For instance, investigations on both humans and animals have found that Bifidobacterium longum reduces stress-induced gut dysfunction, whereas Lactobacillus rhamnosus controls behavioural emotions by increasing GABA

receptors in the brain.[20]

6. SHORT CHAIN FATTY ACID CHAIN: The fermentation of dietary fibres by gut bacteria that produces short-chain fatty acids (SCFAs), mainly acetate, propionate, and butyrate. These metabolites are essential for supporting the integrity of the intestinal barrier, managing immunological responses, and controlling brain activity.[21]

7. NEUROTRANSMITTER

Many neurotransmitter influences by probiotic and probiotics

7.1. Serotonin: About 90% of serotonin is made in the gut, and it is directly related to mood, appetite, and sleep. By influencing tryptophan metabolism and activating enterochromaffin cells, gut bacteria affect the formation of it.[22]

7.2. GABA: The main inhibitory neurotransmitter in the brain is GABA. According to research, some microorganisms may be able to manufacture GABA or control its levels, which could affect behavioural reactions and anxiety.[23]

7.3. Dopamine, Norepinephrine, and Acetylcholine: Important modulators of memory, motivation, and stress, including as dopamine, norepinephrine, and acetylcholine, can be produced or influenced by gut microbes.[24]

8. ANIMAL STUDIES

Animal studies have been instrumental in uncovering the mechanisms by which prebiotics and probiotics influence the gut– brain axis. These studies allow researchers to explore causal relationships between gut microbiota, neurochemistry, and behavior, often under controlled conditions that cannot be replicated in humans. Below are some key findings from research:

8.1. Stress/Anxiety and Probiotics (Rodent Studies): Bravo et al. (2011) showed in one of the most frequently cited research that supplementing mice with Lactobacillus rhamnosus (JB-1) changed the expression of GABA receptors in many brain areas. Significantly, the benefits of this modulation were reliant on vagus nerve signalling and were linked to decreased anxiety-like and depressive-like behaviour. This discovery demonstrated a direct mechanistic connection between a probiotic strain and its regulation of neurotransmitters in the brain.[25]

8.2. Depression Models and Probiotics: Bifidobacterium infantis 35624 shows profound impact in research with animals of depressive disorders. Rats exposed to parental separation (a model of early-life stress resulting in depressive behaviour) showed improved behaviour, decreased pro-inflammatory cytokines, and normalised HPA axis activity after receiving this probiotic strain, according to Desbonnet et al. (2008). This implies that it may be used as a supplemental therapy for depression brought on by stress.[26]

8.2 Gut Inflammation and Neuroinflammation: In comparison to normal mice, studies conducted on germ-free mice (those lacking intestinal microbiota) show a greater response to stress and altering neurological chemistry. Incorporating prebiotics or probiotics into these models prevents microglial overactivation, which is connected to neurodegenerative disorders, and lowers systemic inflammation. Erny et al. (2015), for instance, showed that microglial growth and activity in the brain are regulated by microbial metabolites, specifically SCFAs.[27]

9. CLINICAL TRIALS

9.1 Bifidobacterium longum NCC3001(Patients with IBS & Anxiety)

Study Design: Randomised controlled study in people with co-occurring anxiety along with irritable bowel syndrome(IBS).

Results: Comparing to a placebo, consuming probiotic supplements for six weeks considerably improved quality of life and decreased anxiety levels.[28]

9.2 Lactobacillus plantarum PS128 (Children with Autism, Anxiety Symptoms)

Study design: Open-label research is the study design.

Results: Little ones with autism spectrum disorder (ASD) showed transformations in social habits, sleep quality, and anxiety-related symptoms when taking supplements.[29]

9. PREBIOTIC AND COGNITIVE FUNCTION

Mood and Cognitive Effects of Fructooligosaccharides (FOS) and Inulin

Inulin and FOS supplementation's outcomes for normal individuals were examined in a randomised supervised experiment. The results demonstrated notable gains in attention-related tasks, subjective well-being, and handling emotions. These results imply that prebiotics can alter gut microbiota in a positive way, improving mental and physical health.[30]

Polydextrose (PDX) – Cognitive Improvements in Women: Another double-blind, placebocontrolled crossover study looked at how the water-soluble prebiotic fibre polydextrose (PDX) impacted young, healthy women. Participants demonstrated slight but discernible gains in gut-brain connection and cognitive test performance following four weeks of treatment. This implies that by encouraging SCFA synthesis and microbial diversity, prebiotic fibres may help memory and executive function. [31]

10. PSCYCOBIOTICS

Psychobiotics are a class of probiotics (and certain prebiotics) that interact with the gutbrain-microbiota axis and boost emotional wellness when consumed in sufficient stages. These advantages may include greater mood, increased resilience to stress, decreased anxiety, and better memory.[32]

Production of Neurotransmitters: Some strains, such as Bifidobacterium longum and Lactobacillus rhamnosus, synthesise intermediates of dopamine, serotonin, and GABA that regulate brain activity.

HPA Axis Modulation: Restore balanced stress responses by lowering cortisol release during stress.

Anti-inflammatory Effects: Reduce microglial activation and systemic inflammation to safeguard neurones.

SCFA Production: Increase butyrate levels, which have mood-stabilizing and neuroprotective properties.[33]

11. RESEARCH GAP

11.1 Lactobacillus rhamnosus and GABA modulation: Animal studies shoe effect on GABA receptor expression, reduced anxiety-like behavior Short-term studies, few human clinical trials, and inconsistent dosage Human-level data is necessary to prove the psychiatric effects of GABA, a crucial inhibitory neurotransmitter, in practical applications.

11.2 Properties of a probiotic formulation Lactobacillus helveticus and Bifidobacterium longum in rats and human Some strains lessen depression symptoms via modifying serotonin and reducing inflammation. Strain-specific processes and the lack of extensive, placebocontrolled trials Clinical advice is unclear and may not be useful if it is unclear which strains do what.

11.3 The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems

Microbial metabolites (tryptophan, bile acids, and SCFAs) interact with the central nervous system, the vagus nerve pathway has been found Incomplete mapping of the specific molecular signalling pathways. These could aid in the development of prebiotic and tailored psycho biotic treatments.

The above limitations in the scientific understanding and clinical application of prebiotic and probiotic in gut and brain axis. Connecting these gaps can bring up new treatment prospects in mental health and neurological research.

12. FUTURE OF MICROBIOME-BASEDTHERAPIES

This field has evolved due to new discoveries like microbiome editing (precise methods to change the structure of microorganisms), postbiotics (beneficial microbial metabolites like short-chain fatty acids), and customised gut health therapies. By customising treatments to each patient's distinct microbiome composition, these approaches seek to address both psychological and metabolic health. This field of study is developing quickly and has the potential to completely change the way we treat complicated illnesses including diabetes, obesity, anxiety, and depression.[34]

13. CONCLUSION

The connection between the gut and the brain is now seen as one of the most exciting areas of research in modern medicine. Probiotics and prebiotics are showing real potential in supporting mental well-being, improving mood, and even enhancing memory and learning. They work through many pathways— by producing neurotransmitters, strengthening the gut barrier, lowering

inflammation, and creating metabolites like short-chain fatty acids that protect the brain.

At the same time, research in humans is still catching up. Many of the most promising results come from animal studies, while clinical trials in people remain limited and often vary in design and outcomes. To move forward, scientists need to identify which strains and fibers work best, understand the exact mechanisms, and run larger, long-term studies.

Looking ahead, the future seems hopeful. Advances such as postbiotics, microbiome editing, and personalized nutrition may completely change the way we treat conditions like depression, anxiety, and even metabolic diseases. The gut–brain axis is not just a scientific curiosity—it could soon become a central part of how we care for both body and mind.

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