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THE GUT MICROBIOTA–SEROTONIN AXIS: A NOVEL THERAPEUTIC TARGET IN IRRITABLE BOWEL SYNDROME

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ABSTRACT

Irritable Bowel Syndrome (IBS) is one of the commonest functional diseases affecting the digestive system. Recent research focuses on the interaction between the gut microbiome-serotonin axis and its role in the gut-brain axis. Serotonin (5-HT), produced primarily in the gut, regulates intestinal movements and secretion processes and provides sensory information about visceral stimuli. An imbalance in the gut microbiome causes abnormal levels of serotonin production, resulting in dysfunctions within the gastrointestinal tract. This article will look at various components of the gut microbiome and its role in health and disease, as well as the mechanism of serotonin production and function. Interventions based on the above knowledge can be used to manage patients suffering from IBS.

KEYWORDS: An imbalance in the gut microbiome causes abnormal levels of serotonin production, resulting in dysfunctions within the gastrointestinal tract.

INTRODUCTION

Irritable Bowel Syndrome (IBS) is a functional chronic disorder of the gastrointestinal tract involving symptoms such as abdominal pain, bloating, and changes in bowel movements. It is estimated to affect up to 10 to 15 percent of the world's population. IBS is increasingly considered as a syndrome resulting from an interplay between the brain, gut, and gut microbes, with the neurotransmitter serotonin being one of the important mediators. Up to 90 percent of the body's serotonin is produced in the gut by the enterochromaffin cells, whose production and release are affected by gut microbes.[1]

Pathophysiology

Pathophysiology of Irritable Bowel Syndrome (IBS) is multifaceted, involving an intricate interaction between the gut, brain, and microbiota. Gut-brain-microbiota axis serves as a two-way communication network where dysbiosis affects signaling processes in terms of neuroendocrine, immune, and metabolic systems, resulting in abnormal gut motility and hypersensitivity.

Serotonin (5-HT) acts as the most important neurotransmitter regulating the function of gastrointestinal tract; about 90% of its production occurs through tryptophan hydroxylase-1 (TPH1) in enterochromaffin (EC) cells. 5-HT_3 and 5-HT_4 receptors control motility, secretion, and visceral sensitivity to pain. The imbalance in serotonin transport protein (SERT) results in impaired 5-HT transport, causing variations of serotonin function in different subtypes of IBS; higher serotonin activity is found in IBS-D, lower in IBS-C, while IBS-M displays oscillations of serotonin function.

Regulation of serotonin synthesis takes place due to modulation of tryptophan degradation by the gut microbiota and activation of short chain fatty acids (SCFAs)-dependent EC-cell 5-HT secretion. Moreover, dysbiosis leads to gut wall inflammation, cytokines signaling disturbance, and activation of vagal and hypothalamus-pituitary-adrenal (HPA) axis, thus affecting 5-HT-gut-brain interactions.[2]

Clinical Manifestations and Diagnostic Criteria

The clinical features of IBS include chronic abdominal pain, bloating, and alterations in bowel habit or stool form. Such symptoms typically exacerbate postprandially and resolve with bowel movement, indicating gut dysmotility and increased visceral sensitivity. Extra-intestinal symptoms including fatigue, anxiety, depression, and insomnia are prevalent, underscoring the importance of the gut-brain connection in IBS. According to the Rome IV classification criteria, which is widely accepted in the medical community for diagnosing IBS, IBS is defined as chronic abdominal pain occurring, on average, one or more days per week in the last three months, along with two or more of the following: related to defecation, changes in stool frequency, or changes in stool form. Subtypes of IBS are categorized based on stool appearance by employing the Bristol Stool Form Scale, which comprises four categories: IBS-D (diarrhoea-predominant), IBS-C (constipation-predominant), IBS-M (mixed) and IBS-U (unclassified).[3]

Composition and Functions of the Gut Microbiota

Microbial flora of the gut includes a very heterogeneous group of organisms, which include bacteria, viruses, fungi, and archaea. The bacteria found in the gut belong to four dominant groups, namely Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria, while there are other rare forms such as Verrucomicrobia. The presence of these microbes in the gut depends on the location within the gut and factors such as nutrition, age, and environmental conditions.

Regarding its functions, the gut microbiota is responsible for establishing the balance in the intestines and thus ensures the wellbeing of the organism. It promotes the digestion and fermentation of dietary fibers resulting in the production of short-chain fatty acids (acetate, propionate, butyrate) used by colonocytes for energy production and contributing to maintenance of mucosal integrity. Apart from that, the gut microbiota supports vitamin synthesis (B complex, K) and influences bile acid metabolism while providing protection from colonization by pathogenic microorganisms. Not only does the gut microbiota affect digestion; it also impacts the functioning of the immune system, promoting immunotolerance through signaling via receptors of microbial components. Most importantly, it is in constant communication with the central nervous system via neural, endocrine, and immune channels. The gut microbiota forms part of the gut-brain axis, and its alteration causes dysbiosis associated with various diseases, e.g., Irritable Bowel Syndrome (IBS).[4]

Microbiota-Derived Metabolites and Neurotransmitters

Several metabolites and neurotransmitters are synthesized by the gut microbiota, and they have significant functions in maintaining balance in the gastrointestinal and nervous system. The short-chain fatty acids (SCFAs), which include acetate, propionate, and butyrate, are important metabolites synthesized by fermentation of the dietary fibers in the gut to help regulate intestinal barrier function, immune responses, and secretion of 5-HT in the EC cells. Additionally, the gut microbes modulate tryptophan catabolism in either the kynurenine or serotonin pathway, leading to changes in gut motility, mood, and pain. Neurotransmitters synthesized by several microbes like Lactobacillus, Bifidobacterium, and Escherichia are GABA, dopamine, acetylcholine, and norepinephrine. They affect the enteric and central nervous system in interaction with the immune system via the vagus nerve. These metabolites and neurotransmitters play an important role in the gut-brain-microbiota axis that is essential for both gastrointestinal and behavioral functioning.[5]

Serotonin (5-HT) Signaling in the Gut

Serotonin (5-hydroxytryptamine, 5-HT) is one of the essential neuromodulators involved in GI motility, secretion, and visceral sensory function. Roughly 90% of serotonin in the body is synthesized from tryptophan by tryptophan hydroxylase-1 (TPH1) in enterochromaffin (EC) cells lining the intestines, while the other 10% is generated by the enteric nervous system (ENS). Serotonin is released from EC cells following activation and acts on certain 5-HT receptor subtypes (e.g., 5-HT_3 and 5-HT_4) present in enteric nerves, smooth muscle, and epithelial cells, controlling contraction, secretion, and pain signaling. Serotonin transporter (SERT) recaptures 5-HT from extracellular space to prevent homeostatic imbalance; any change in the expression or activity of SERTs causes dysmotility and increased sensitivity observed in Irritable Bowel Syndrome (IBS). Additionally, serotonin production and metabolism depend on the gut microbiome because certain SCFAs and products of tryptophan metabolism are used for serotonin synthesis, forming an important microbiota-serotonin axis.[6]

Synthesis and Metabolism of Serotonin in the Enteric Nervous System

Serotonin (5-hydroxytryptamine, 5-HT) is a critical neurotransmitter involved in gut motility, secretion, and sensory processing within the enteric nervous system (ENS). Serotonin synthesis starts with the hydroxylation of tryptophan, an essential amino acid, by tryptophan hydroxylase (TPH); TPH1 catalyzes tryptophan hydroxylation in EC cells, while TPH2 does so in enteric neurons, forming 5-hydroxytryptophan (5-HTP) that is further decarboxylated by aromatic L-amino acid

decarboxylase (AADC) to generate serotonin. Released serotonin activates different types of 5-HT receptors to participate in the regulation of peristalsis and visceral sensitivity. Serotonin is removed from synaptic spaces through the action of the serotonin transporter (SERT), present in enterocytes and enteric neurons, and terminated intracellularly via monoamine oxidase (MAO) degradation, forming 5-hydroxyindoleacetic acid (5-HIAA) that is eliminated in urine. Changes in serotonin levels due to altered expression of TPH, impaired SERT, or the effect of bacteria on tryptophan metabolism may result in abnormalities in gastrointestinal motility and sensitivity characteristic of Irritable Bowel Syndrome (IBS).[7]

Role of Serotonin in Gut Motility and Sensation

Serotonin (5-hydroxytryptamine; 5-HT) plays an important role in the modulation of both gut motility and sensation, mediating the interaction between EC cells, enteric neurons, and the smooth muscles. Following a physical or chemical stimulus, EC cells secrete 5-HT, activating intrinsic primary afferent neurons (IPANs) and enteric motor neurons via 5-HT_3 and 5-HT_4 receptors, resulting in peristaltic and secretomotor responses required for the proper functioning of the gastrointestinal tract. Increased 5-HT secretion enhances motility, while decreased serotonin secretion causes delayed transit and causes constipation. In addition, serotonin affects visceral sensitivity because of its actions at sensory nerve endings projecting to the central nervous system, affecting the experience of pain and the gut-brain interaction. The aberrant serotonin signaling that can be due to inappropriate release of serotonin, 5-HT receptor function, and serotonin transporter (SERT) leads to motility disturbances and visceral hypersensitivity observed in IBS.[8]

Methodological Considerations in Studying the Axis

To study the gut microbiota-serotonin axis, an interdisciplinary strategy involving microbiology, neurogastroenterology, and molecular biology should be adopted. The investigation of this axis raises many methodological challenges due to the complexity of the research topic. The evaluation of the microbial composition in fecal samples with 16S rRNA gene sequencing or metagenomics may shed some light on the microbial composition in the gut; however, this method does not necessarily correlate with the presence of mucosa-associated microbiota. The analysis of the serotonin concentration in the plasma, tissue, or stool also needs to take into consideration its fluctuations in accordance with the circadian rhythms as well as the quick degradation of serotonin molecules. The role of the gut microbiota in serotonin synthesis has been elucidated with the help of in vitro methods (EC cells cultures and organoids) and animal models. However, the combination of new multi-omics approaches (metabolomics and transcriptomics), which could reveal the entire picture of interaction between microbiota, receptors, and host response, is currently the best way to study the gut microbiota-serotonin axis.[9]

DISCUSSION

Understanding the gut microbiota-serotonin (5-HT) axis in Irritable Bowel Syndrome (IBS) is critical in explaining the underlying pathophysiology of this condition, whereby the microbial community affects both gut and brain functions through its regulation of serotonin. In particular, serotonin acts as an important modulator in the regulation of intestinal motility, secretion, and visceral sensitivity, whereas the gut microbiota influences the production and metabolism of serotonin by controlling tryptophan and microbial metabolites like short-chain fatty acids (SCFAs). Imbalance within the 5-HT axis, caused by microbial dysbiosis, results in dysfunctional 5-HT signals, leading to symptoms of IBS, such as abdominal pain and constipation.

Despite considerable advancements in the field, a clear understanding of how this axis functions is yet to be achieved because of the complexity associated with IBS and variation in microbiota across different individuals.[10]

CONCLUSION

The gut microbiota-serotonin axis is an exciting, novel target for the treatment of IBS. Alteration of this axis using microbiota-based treatments such as probiotics, prebiotics, diet manipulation, antibiotics, and FMT in conjunction with serotonergic medications like 5-HT3 antagonists and 5-HT4 agonists will make personalized medicine possible. Knowledge of this two-way communication system will revolutionize IBS treatment by moving away from symptomatic treatments to specific mechanisms involving gut-brain-microbiota modulation. Further research needs to be focused on converting this knowledge into a beneficial treatment modality.

REFERENCES

1. Yano JM, Yu K, Donaldson GP, Shastri GG, Ann P, Ma L, et al. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell, 2015; 161(2): 264–276.
2. O'Mahony SM, Clarke G, Borre YE, Dinan TG, Cryan JF. Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. Behav Brain Res, 2015; 277: 32–48.
3. Mishima Y, Yamaguchi Y, Hikichi Y. The role of serotonin in the pathophysiology of irritable bowel syndrome and other gastrointestinal disorders. *Int J Mol Sci, 2021; 22(19): 10235.
4. Raskov H, Burcharth J, Pommergaard HC. Irritable bowel syndrome, the microbiota and the gut-brain axis. Postgrad Med J, 2016; 92(1090): 414–420.
5. Chen M, Wang Q, Chen Y. Gut microbiota and the regulation of serotonin metabolism: Implications for

the gut–brain axis and metabolic disorders. Front Endocrinol (Lausanne), 2022; 13: 817100.
6. Barandouzi ZA, Lee J, Rosas MC, Welch M, Ballou S, Chang L, et al. Altered gut microbiota and tryptophan metabolism in irritable bowel syndrome patients. Sci Rep, 2022; 12: 1648.
7. Mujagic Z, Friedrich M, Vork L, van den Heuvel TRA, van den Bogert B, El Aidy S, et al. Microbiota–gut–brain axis biomarkers in irritable bowel syndrome. Microbiome, 2022; 10(1): 206
8. Akram N, Symonds E, Arpana T. Gut microbiota modulation and serotonin regulation in irritable bowel syndrome: A review. *Food Sci Nutr.* 2024; 12(4): e3826.
9. Everett BA, Goldstone AP, Sanders DS, Aziz Q. Serotonin signaling and its interaction with the gut microbiota in irritable bowel syndrome. Neurogastroenterol Motil, 2022; 34(9): e14328.
10. Clarke G, Sandhu KV, Griffin BT, Dinan TG, Cryan JF, Hyland NP. Gut reactions: Breaking down xenobiotic–microbiome interactions. Pharmacol Rev, 2019; 71(2): 198–224.