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Review Article

GUT MICROBIOTA–BRAIN AXIS IN NEUROLOGICAL DISORDERS

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Abstract: The gut microbiota–brain axis (GBA) is a bidirectional communication system between the gut and the central nervous system (CNS) that includes neural, endocrine, immune, and metabolic pathways. Evidence shows that alterations in the gut microbiota, contribute to the pathogenesis and progression of various neurological disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS) and stroke. This review presents the GBA and its role in neurological health and disease. We also discuss therapeutic approaches, including dietary interventions, probiotics, and fecal microbiota transplantation.

Keywords: Gut microbiota, Neurological disorders

INTRODUCTION

The gut microbiota comprises trillions of microorganisms, including bacteria, fungi and viruses which reside in the gastrointestinal (GI) tract. This complex ecosystem of microorganisms influences the local gut physiology and also exerts effectson the CNS. Gut microbiome connects the gut health to brain function via neural, endocrine, immune, and metabolic pathways [1].

The alteration of microbial composition and diversity is implicated in playing a role in the pathogenesis of neurological disorders. Understanding the GBA offers novel insights into disease mechanisms and therapeutic opportunities for managing neurological conditions.

Mechanisms of the gut microbiota–Brain axis

Neural pathways: The vagus nerve plays a critical role in transmitting signals from the gut to the brain. Microbial metabolites, such as short-chain fatty acids (SCFAs), interact with the vagus nerve to modulate CNS functions, including stress responses and neuroinflammation [2].

Immune pathways: Gut microbes regulate the production of cytokines and other immune mediators, influencing systemic inflammation and the integrity of the blood-brain barrier (BBB). Alteration in the gut microbiome can lead to increased permeability of the BBB, thus facilitating neuroinflammation [3].

Endocrine pathways: The hypothalamic-pituitary-adrenal (HPA) axis is influenced by gut microbiota through the production of neurotransmitters and hormones [4]. For instance, serotonin, predominantly synthesized in the gut, plays a crucial role in mood regulation and cognitive function [5].

Metabolic pathways: SCFAs, derived from microbial fermentation of dietary fibers, modulate brain function by regulating neurotransmitter synthesis and neuronal plasticity [6].

Role of gut microbiota in neurological disorders

Alzheimer's disease (AD): AD is characterized by amyloid-β plaque accumulation and neuro-inflammation. Studies have shown that certain bacterial groups such as Escherichia and shigella which play a role in mediating inflammation, are increased in faecal samples in patients with AD compared with healthy individuals**.** The microbiota changes in patients with Alzheimer's disease were associated with pro-inflammatory cytokine concentrations [7].

Parkinson's disease (PD): In PD, the pathology begins the in the gut. Alpha synuclein, the protein aggregate that is the hallmark of PD has been found been identified in the mucosal and submucosal nerve fibres and ganglia [8]. Studies have shown alterations in the composition of the microbiota in patients with Parkinson's disease [9].

Gut microbiota is crucial for the development and maturation of the immune system [10]. Children that have MS have subtle, discrete taxonomic changes, of the gut microbiota as compared to healthy controls [11]. In another study, the transgenic mice were administered with MS twin-derived microbiota which led to significantly higher incidence of auto-immunity than the healthy twin-derived microbiota [12].

Autism spectrum disorder (ASD): It has been observed that more than 50% of the neurobiology of autism is driven by non-heritable factors [13]. Many studies have demonstrated alterations in the composition of the microbiota in ASD [14].

Therapeutic Strategies Targeting the Gut Microbiota:

Probiotics and prebiotics: Probiotic strains, such as *Lactobacillus* and *Bifidobacterium*, improve gut health and modulate neuroinflammatory pathways [14]. In a randomized controlled trial prebiotics were used in to show improvement in bowel movements in PD patients [15].

Dietary interventions: Dietary patterns significantly influence gut microbiota composition. Dietary intervention in a MS model led to reversal of loss of the integrity of the damaged blood brain barrier. These foods were rich in SCFA or bacteria producing SCFAs [16].

FMT involves transferring microbiota from healthy donors to patients. Preliminary studies indicate its potential in restoring microbial balance and improving neurological outcomes in manu diseases such as PD, MS. In an animal study FMT reduced gut microbial dysbiosis, decreased fecal SCFAs, alleviated physical impairment, and increased striatal DA and 5-HT content of PD mice [17]. FMT has also been investigated in the treatment of ASD [18]. In an open label trial in ASD patients, FMT 47 to 8 weeks following antibiotic therapy led to improvement in GI and behavioral symptoms of ASD [19].

Pharmacological approaches: Antibiotics and microbial-derived metabolites are being investigated for their neuroprotective effects. An expanding body of evidence supports the notion that microbes can metabolise drugs and conversely drugs can modify the gut microbiota composition leading to alteration of disease profile [20].

CONCLUSION

The GBA represents a paradigm shift in understanding the pathophysiology of neurological disorders. Targeting the gut microbiota offers a novel, multidimensional approach to disease management. Further research is required to develop personalized microbiota-based therapies based on individual gut microbiome.

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