THE INTESTINAL MICROBIOTA
Leader of our behavior and health

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INTRODUCTION

There is a bidirectional communication between the central nervous system (CNS) and gastrointestinal tract (GIT), which are communicated through the vagus nerve and the hypothalamo-pituitary-adrenal (HPA) axis. Recent years have witnessed the rise of the gut microbiota as a key factor in this communication, contributing to maintain the homeostasis and influencing the brain function and behavior. The deregulation of this axis could lead to a variety of disorders like irritable bowel syndrome (IBS), stress, obesity, pain, autism and multiple sclerosis. This emerging concept suggests therapeutic opportunities in which the gut microbiota represents a tractable strategy for the management of complex CNS disorders.

OBJECTIVES

This review aims to:
1. Introduce the basics and relationship of brain-gut-microbiota axis.
2. Describe the importance of intestinal microbiota, mechanisms of action and their influence on the CNS and health.
3. Introduce therapeutic applications with the goal of treating CNS disorders.

INTESTINAL MICROBIOTA

The GIT is inhabited with \( 10^{14} \) microorganisms, with 1,000 species and more than 7,000 strains. The microbiome 70–75% is defined by two phyla, Bacteroidetes and Firmicutes. There is a significant interindividual variation in the entire microbiota, but there seems to be a balance that confers health benefits and an alteration can negatively influence the wellbeing of the individual. Several factors may alter the microbiome such as infection, disease, diet, and antibiotics.

FUNCTIONAL RELEVANCE OF THE MICROBIOTA

The studies with germ-free (GF) animals have offered the most revealing insights about function of the microbiota.

The microbiota is essential for:
- Normal GIT motility and maintenance of intestinal barrier function.
- Expression of TLR family in GIT.
- Development of the gut associated lymphoid tissue (GALT) and IgA secretion.
- Support normal digestion and host metabolism (a significant energy source for humans is the bacterial metabolite short-chain fatty acids (SCFAs)).
- Prevention of colonization by pathogens.

MICROBIOTA AND CENTRAL NERVOUS SYSTEM

The microbiota uses a huge variety of mechanisms to influence CNS function, the vagus nerve and tryptophan metabolism are the most important. The other mechanisms are:
- Altering microbial composition
- Immune activation
- Microbial metabolites
- Microbial neurometabolites
- Bacterial cell wall sugars

There are different pathways involved in bidirectional communication between the gut microbiota and the brain. The neuroimmune and neuroendocrine systems, the autonomic nervous system (sympathetic and parasympathetic) and the enteric nervous system are the pathways that allow the communication between the gut microbiota and the CNS.

BIDIRECTIONAL INFLUENCE BETWEEN MICROBIOTA AND CNS IN STRESS

The HPA axis is the endocrine core of the stress system; recent studies demonstrated that the composition of the intestinal microbiota influences the development of an appropriate stress response later in life. Moreover, there is a critical window in early life which colonisation must occur to ensure normal development of the HPA axis.

At the neuronal level, GF animals had:
- Brain-derived neurotrophic factor (BDNF)
- NMDA receptor subunit 2A (NR2A)
- Serotonin receptor 5-HT 1A

The CNS can also alter the microbiome. The stress induces changes in the molation, secretion and intestinal permeability, thus altering the GIT environment in which bacteria reside what in turns alters the composition of the microbiome.

INFLUENCE OF THE MICROBIOTA IN INTESTINAL DISORDERS

Irritable bowel disease (IBS) is a disorder with a GIT microbial signature although it isn’t clear whether these changes are responsible for causing this disease. The changes in the microbiota are characterized by increases in Proteobacteria and a decline in Firmicutes and Bacteroidetes. Although the pathogenesis is still not completely understood, it is clear that the psychological stress, a factor which can perturb the microbiota, exacerbates the condition.

The best evidence to date the involvement of the microbiota in disease states comes from irritable bowel syndrome (IBS). There is a role of the microbiota in the pathophysiology of IBS which describes the development of IBS following an episode of bacteriologically confirmed gastroenteritis (post-infectious IBS).

THE MICROBIOTA IN CNS-RELATED CONDITIONS

The microbiota composition is involved in some behavioral disorders such as stress, anxiety and depression. However, this composition of gut microbiota may also have a role in several other conditions that involve the CNS.

THERAPEUTIC OPPORTUNITIES OF PROBIOTICS

Probiotics are emerging as potential therapies for stress-related gastrointestinal disorders such as IBS, reducing the anxiety and stress response and improving mood in IBS patients. The mechanisms by which probiotics works is a very complex network of events like displacement of pathogens, production of bacteriocins, enhancement of mucosal barrier function and modulation of the immune system.

CONCLUSIONS

The intestinal microbiota plays an important role in the communication between the CNS and the TGI, it has consequences in our health and in some aspects of our behavior. Changes in intestinal microbiota or lack of it in germ-free animals involves a wide range of problems such as an increase in response to stressors, lower likelihood of obesity, worse development of the immune system and higher probability to develop irritable bowel disease.

The communication between the brain-gut-microbiota in health and disease, still require a broad understanding of the intervention of the intestinal microbiota and fully be able to differentiate between normal microbiota and which is found during a disease. The discovery of the influence of the intestinal microbiota in different aspects of behavior and health leads to suggest new therapeutic applications as the use of probiotics to solve some disorders.

REFERENCES