BMH MEDICAL JOURNAL

BMH Med. J. 2022;9(4):80-83. **Brief Review**

Effects and Potentials of Bidirectional Communication Between Gut & Brain - A Review

Elizabeth KE

UNICEF Consultant, Kerala

Address for Correspondence: Dr. Elizabeth KE, MD, DCH, PhD, FIAP, FRCPCH (UK), Professor and HOD Pediatrics, Sree Mookambika Institute of Medical Sciences, Kanyakumari, India. Email: drelizake@gmail.com

Abstract

The bidirectional Gut-Brain Axis is now identified as a key factor for growth, development and emotions. In fact, it is the gut microbiome and certain nutrients that communicate to the brain and direct the brain in several ways. The gut microbiome also communicates to the immune system and plays a vital role in maintaining health. This review article brings out the intricacies of Gut- Microbiome-Brain Axis, its modulation, and the role of nutrition interventions for selected Disorders of Gut Brain Interactions (DGBIs).

Keywords: nutrition, gut-brain axis, gut brain interaction, gut-microbiome-brain axis, disorders of gut brain interactions, DGBI

Introduction

"One day the body parts were fighting each other as to which is the most important organ. Each organ stated its respective importance. The brain said it controls everything. The heart said its beating keeps life going. The Lungs said its breathing brings oxygen. The liver highlighted its synthetic, secretory and detoxifying functions. Finally, the gut said, without its digestion, absorption and gut heath, life cannot be sustained. Every other organ laughed aloud. And the gut got very angry and shut all its function. In a few days, all organs agreed to the claim of the Gut". Thus, the story goes.

It is interesting to note that that, Hippocrates, the Father of Modern Medicine, had endorsed the claim of the gut. According to him, "All diseases begin in the gut and Health is determined by the microbiota in the Gut".

Are we Homo sapiens or Micro sapiens?

There are a greater number of microbiomes in the human body, 10^{14}, which is more than the number of cells in the body. There are billions of microbes living in the gut, mouth and skin and we humans depend upon the microbiomes to function and maintain health and well-being. Microbiomes contribute about 2 Kg weight and 3 million genes to humans.

Which are the Gut Microbiomes?

Microbes include bacteria, viruses, fungi, algae, and protozoa. Most bacteria belong to the genera Bacteroides, Clostridium, Faecalibacterium, Eubacterium, Ruminococcus, Peptococcus, Peptostreptococcus, and Bifidobacterium. Other genera, such as Escherichia and Lactobacillus, are present to a lesser extent. Species from the genus Bacteroides alone constitute about 30% of all bacteria in the gut, suggesting that this genus is especially important in the functioning of the host. These communicate to the brain via Gut Brain Axis. These also orchestrate the Immune system.

Factors that decide Body and Gut Microbiome [1,2,3]

Factors that influence Gut Bacterial Composition are several including the environment, diet, infections, medications and genetics. The home environment, the place of birth, and the type of delivery are the key factors. Infant feeding, especially human milk or bovine milk or commercial preparations is an important factor for establishing the bacterial community in the gut.

Milk is Species Specific and factors in Breastmilk that promote favourable microbiota. The early life period is a "window of opportunity" to program health through microbiota modulation. Breastmilk is a treasure of Prebiotics, Probiotics & Postbiotics that modulate gene expression via Epigenetic mechanisms. Specific human milk oligosaccharide (HMO) promote Bifidobacterium species that dominate the ecosystem as long as the infant is primarily breastfed.

Role of Microbiota

There are 3 Major Functions, Protective, Structural and Metabolic like Fermenting dietary Fibre into short chain fatty acids (SCFA) and synthesis of Vitamins. These perform saccharolytic fermentation to short chain fatty acids in the gut and offer protection against infectious and immune-related diseases. There is evidence that the composition of the gut microbiota influences metabolism and can affect energy balance, gut permeability, and inflammation. These microbial metabolites act as a messenger in the brain-gut axis and are correlated with a reduction in anxiety and depression.

Other Specific Factors that influence the gut microbiota of the infant

Omega 3 Fatty acids have a proven role in restoring and maintaining healthy intestinal microbiota, and reducing intestinal inflammation. The major long chain Polyunsaturated fatty acids (LCPUFAs) that are derived from Omega 3 Linolenic acid are DHA & EPA, which are brain and heart friendly. DHA also promotes the development of short-chain fatty acid-producing bacteria and reduce pro-inflammatory molecules. In addition to acting on the microbiota, DHA has a potentially beneficial role in various gut conditions and colon cancer, by reducing chronic inflammation. Human milk has 30 times more DHA than Cow's milk.

Breastmilk provides a perfect balance between Omega 6 & Omega 3 LCPUFAs, of which Omega 3 (Linolenic) leading to DHA & EPA, which are Anti-inflammatory and Omega 6 (Linoleic) leading to Arachidonic & Adrenic Acid, which are Pro-Inflammatory. The desired Omega 6: Omega 3 Ratio (n6: n3) is <5-10:1)

What is meant by Leaky Gut?

Leaky gut syndrome is based on the theory that intestinal permeability is not only a symptom of gastrointestinal disease, but an underlying cause that develops independently. If the intestinal barrier is impaired or immature, it may be letting toxins, antigens, proteins and polypeptides into the bloodstream. Leaky gut, or increased intestinal permeability, occurs when the tight junctions of intestinal walls loosen. This may allow harmful substances, such as bacteria, toxins, and undigested food particles, to pass.

Proponents claim that a "leaky gut" causes chronic inflammation throughout the body that results in a wide range of conditions, including chronic fatigue syndrome, rheumatoid arthritis, lupus, migraines, multiple sclerosis, and autism. However, till date, this is not convincingly proven.

Bidirectional Gut Brain communication [4,5]

The gut-brain axis is a bidirectional communication system between the central nervous system (CNS) and the GI tract. Gut microbes communicate to the CNS through at least Three parallel and interacting channels involving nervous, endocrine, and immune signalling mechanisms.

There are many potential direct and indirect pathways through which the gut microbiota can communicate and modulate the gut-brain axis. These include endocrine (cortisol), immune (cytokines), and neural (vagus and enteric nervous system) pathways.

Communication pathways include sensory neurons, cytokines, gut hormones and microbial factors, that signal from the gut to the brain where these can modify cerebral function and behaviour. There are two pathways, autonomic and neuroendocrine outputs, that signal from the brain to the gut.

Regulation of the microbiota-brain-gut axis is essential for maintaining homeostasis, including the CNS. The microbiota-gut-brain axis leads to communication and interaction of enteric and central nervous system that decide emotional and cognitive functions.

The brain-gut-microbiota axis is modulated by the enteric microbiota.

Thus, Both Microbes & DHA modulate brain function. Both human and animal studies have highlighted the ability of omega-3 PUFAs to influence the gut-brain axis, acting through gut microbiota composition.

How are Neurotransmitters related to Microbiota?

Besides short-chain fatty acids and bile acids, recent studies show that the metabolites produced by the gut microbiota also include some neurotransmitters such as glutamate, GABA, serotonin, and dopamine. GABA is synthesized by Lactobacilli, Bifidobacterium, Norepinephrine by Escherichia and Saccharomyces, Acetyl Choline by Lactobacilli and Serotonin by Candida, Escherichia, Enterococci and Streptococci.

What are the Nutritional Interventions useful for Disorders of Gut Brain Interaction (DGBIs)?

Emerging evidence suggests that gut microbes play a crucial role in the brain development and flow of information across the nervous system. Poor gut health may contribute to the onset and progression of depression, anxiety, schizophrenia, autism spectrum disorders, migraine, and epilepsy [6,7].

DGBIs include Irritable bowel syndrome, Reflux hypersensitivity, Functional dyspepsia and many more. These are called DGBIs because these are believed to be due to impaired bidirectional communication between the gut and the brain.

Glutamatergic signaling is another interesting and unique factor to treat DGBIs through dietary intervention via modulation of the gut microbiota.

Autism Spectrum Disorders (ASD) has Gastrointestinal disturbances as comorbidities that are not only another symptom of ASD, but also play an expression of social and behavioral symptoms. Nutritional interventions for ASD, include the following with varying results [8]:

- Gluten-free and Casein-free diet,

- Ketogenic, and specific Carbohydrate diets,
- Polyunsaturated fatty acids,
- Probiotics,
- Dietary supplements and vitamins A, C, B6, B12, D; magnesium and folate

ADHD is yet another condition that may benefit the Gut Bain Interaction. ADHD share symptoms of EFA Deficiency. There are reports of significantly lower levels of plasma Arachidonic acid & DHA in subjects with Severe ADHD than controls and those with fewer symptoms.

Dietary approaches for ADHD include elimination of sugar, candy and food with red dye. The assumption is that being sensitive to certain foods may cause or worsen symptoms of ADHD.

'Nutritional Psychiatry' is an emerging area of research that has great potential as an adjunctive tool for the prevention and treatment of diverse neuropsychiatric disorders.

References

1. Burcelin R. Gut microbiota and immune crosstalk in metabolic disease. Mol Meta. 2016; 5:771-781.

2. Rothe M, Blaut M. Evolution of the gut microbiota and the influence of diet. Benef Microbes. 2013; 4 : 31-37.

3. Wu GD, Chen J, Hoffmann C, Bittinger K et al. Linking long-term dietary patterns with gut microbial enterotypes. Science. 2011; 334: 105-108.

4..Mayer E.A. Gut feelings: the emerging biology of gut-brain communication. Nat Rev Neurosci. 2011; 12:453-466.

5. Rhee S.H., Pothoulakis C., Mayer E.A. Principles and clinical implications of the brain-gut-enteric microbiota axis. Nat Rev Gastroenterol Hepatol. 2009; 6:306-314.

6. Cryan J.F., Dinan T.G. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. Nat Rev Neurosci. 2012; 13:701-712.

7. Park A.J., Collins J., Blennerhassett P.A., Ghia J.E., Verdu E.F., Bercik P., Collins S.M. Altered colonic function and microbiota profile in a mouse model of chronic depression. Neurogastroenterol Motil. 2013;25 733-e575.

8. Vuong H.E., Hsiao E.Y. Emerging roles for the gut microbiome in autism spectrum disorder. Biol Psychiatry. 2017; 81:411-423.