ejpmr, 2022, 9(10), 142-147

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

THE MICROBIOTA-GUT-BRAIN AXIS AND MENTAL HEALTH

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Article Received on 24/07/2022 **Article Revised on 14/08/2022** **Article Accepted on 04/09/2022**

ABSTRACT

Ever had butterflies in the stomach or a gut feeling? These stomach's feelings reflect a connection between our brain and gut. Additionally, current research indicates that gut health may even have an impact on the health of our brain and vice-versa. The gut-brain axis is the term used to describe the communication pathway between our gut and brain. The enteric and central nervous systems are connected by a bidirectional communication network called the gut-brain axis. In addition to being anatomical, this network also includes endocrine, humoral, metabolic, and immunological pathways for communication. The brain can regulate intestinal processes, including the activity of functional immune effector cells, through the autonomic nervous system, hypothalamic-pituitary-adrenal (HPA) axis, and nerves in the gastrointestinal tract, whilst the gut can influence mood, cognition, and mental health.

KEYWORDS: Gut- Brain axis, Gut microbiota, Short-chain fatty acids, Stress, IBS, Probiotics, Galanin, Intestinal tight junction.

INTRODUCTION

The network of communication between your gut and brain is known as the gut-brain axis.[1] Clinical, epidemiological, and immunological data support the idea that enteric microbiota has a significant and profound impact on the link between the gut and the brain (i.e., mental state, emotional regulation, neuromuscular function, and regulation of the HPA). Research has shown that variances in the microbiota are connected to changes in these systems of communication and is still elucidating the mechanisms of action to explain the impacts of bacteria, both directly and indirectly, on emotional and cognitive centres of the brain.[2,3]

In contrast to GI disease (such as irritable bowel syndrome or irritable bowel disease) which frequently involve psychological comorbidities associated with alteration of the gut microbiome, various mood disorders such as anxiety, depression, and autism spectrum disorders, now have well-established linkages to functional GI disruptions.[4-10]

Four main pathways of the gut-brain axis—neurologic, endocrine, humoral/metabolic, and immune—have been further clarified by extensive research.

Neurological Pathway

The human brain contains 100 billion neurons on average.[11] It's interesting to note that 500 million of your brain's neurons reside in your gut and are connected to it by nerves in your nervous system.[12]

The Vagus nerve, the enteric nervous system, and the release of neurotransmitters in the GI tract are all parts of the neurologic route. With the aid of the trillions of microbes that reside there, afferent sensory nerves directly produce molecules in the gut cells[13], that can function as local neurotransmitters, such as GABA, serotonin, melatonin, histamine, and acetylcholine. This pathway also produces biologically active forms of catecholamines in the gut lumen.[3] Happiness and body clock regulation are both aided by serotonin[14] and Gamma-aminobutyric acid (GABA) aid in the regulation of fear and anxiety.[15]

Certain probiotics have been demonstrated in studies with laboratory mice to enhance GABA synthesis, which in turn lowers anxiety and depressive-like behaviour.[16] Stress impairs the signals conveyed by the vagus nerve in animal trials and also results in gastrointestinal issues.[17] Similarly, a human study discovered that individuals with Crohn's disease or irritable bowel syndrome (IBS) showed decreased vagal tone, indicating that the vagus nerve was not functioning as well as it should.[18]

In an intriguing study, it was discovered that giving mice a probiotic reduced the level of the stress hormone in their blood. The probiotic had no effect when their vagus nerve was cut, however.[19] This shows that the vagus nerve plays a crucial part in the gut-brain axis and in how stress is processed.

Endocrine Pathway

The gut microbiota impacts the availability of nutrients, which in turn affects how enteroendocrine cells produce physiologically active peptides, which can therefore have an impact on the gut-brain axis. For instance, the neuropeptide galanin is hypothesised to have a role in several important neurobiological processes, such as nociception, control of the sleep–wake cycle, regulation of food, mood, control of blood pressure, and neurotropic processes. Galanin increases the release of corticotrophin-releasing factor and adrenocorticotropic hormone from the central branch of the HPA axis, which in turn increases the production of glucocorticoids from the adrenal cortex.[20] Furthermore, it has the capacity to directly trigger the release of norepinephrine from the adrenal medulla and cortisol from the adrenal cortex, indicating that it plays a role in the HPA axis response to stress.[21]

Humoral / Metabolic Pathway

Numerous additional substances that impact how your brain functions are also produced by the billions of microbes that reside in your gut.[22] Many short-chain fatty acids (SCFAs), including butyrate, propionate, and acetate, are produced by the bacteria in your gut.[23]

They metabolise fibre to produce SCFA. SCFA have a variety of effects on brain function, including hunger suppression. According to one study, taking propionate can lower food intake and lower brain activity associated with rewarding high-energy foods.[24] The formation of the blood-brain barrier, depends on butyrate, another SCFA, and the microorganisms that make it.[25]

Through the disruption of microglial communication and function, alterations in SCFA metabolism have been linked to the development of autism.[26-29]

The manufacture of gut-derived serotonin by enterochromaffin cells and the release of gut peptides from enteroendocrine cells are both regulated by SCFAs, and both of these processes have an impact on the hormonal exchange between the gut and the brain.[30] Serotonin is produced in the gut to a degree of 95% of the body's total, with plasma containing the preponderance.[27] Most doctors aren't aware that children with autism have been found to have increased plasma serotonin levels.[31,32]

Lipopolysaccharide (LPS), which is mostly generated from the cell walls of Gram-negative enterobacteria, is another important bacterial metabolite. Through intestinal epithelial tight junction permeability problems, often known as leaky gut syndrome, LPS enters the systemic circulation. Antibodies against LPS are produced by the human body, and major depressive disorder patients have greater levels of these antibodies than in controls.[33] Numerous brain ailments, including severe depression, dementia, and schizophrenia, have been linked to high blood levels of LPS.[34]

To create additional molecules that have an impact on the brain, gut microorganisms also metabolise bile acids and amino acids.[22] According to two research done on mice, social problems and stress both suppress the synthesis of bile acids by gut bacteria and alter the genes responsible for their production.[35]

Immune Pathway

The gut microbiome has an influence on the metabolism of inflammation in the GI tract, primarily through the immune system's secretion of cytokines (including interleukin [IL]-10 and IL-4) and other cellular communication mediators, such interferon-gamma, during dysbiosis. As an illustration, In irritable bowel syndrome (IBS), aberrant microbiota populations trigger mucosal innate immune responses, increasing gut epithelial permeability, activating gut pain sensory pathways, and dysregulating the enteric nervous system[3,36,37]; both brain-gut and gut-brain dysfunctions occur, with the former being predominate.[38]

Intestinal motility and secretion are impacted by disruptions in the gut-brain axis, which also contributes to visceral hypersensitivity and induces cellular alterations in the immunological, enteroendocrine, and endocrine systems.[3]

Epithelial Barrier Structure and Function

It is now well established that stress changes intestinal epithelial permeability, allowing bacterial antigens and LPS to circulate and have a wide range of consequences.[39-43] Acute stress affects the GI tract by altering colonocyte differentiation and reducing the expression of mRNA encoding tight junction proteins, according to in vivo studies.[44]

Irritable bowel syndrome (IBS), necrotizing enterocolitis, and the low-level inflammation commonly encountered in metabolic syndrome, obesity, and diabetes have all been linked to intestinal permeability defects.[45] It should be unsurprising that taking probiotic supplements may affect intestinal tight junction integrity and aid in the recovery of illnesses brought on by or made worse by a dysfunctional gut barrier.[46,47]

Probiotics, Prebiotics and the Gut-Brain Axis

Altering your gut flora may help your brain function better since gut flora have an impact on brain health. Probiotics are living bacteria that, when consumed, provide health advantages. Probiotics vary in composition, though. Often called "psychobiotics," probiotics that have an impact on the brain.[48] It has been demonstrated that certain

probiotics can reduce stress, anxiety, and depressive symptoms.[49]

One small trial revealed that consuming the probiotic Bifidobacteriumlongum NCC3001 for six weeks significantly reduced symptoms in patients with mild to severe anxiety or depression and irritable bowel syndrome.[50] Changes in gut flora may enhance brain health since gut flora impact brain health. Prebiotics, which are generally fibres that your gut bacteria ferment, may also have an impact on the health of your brain. According to one study, the level of the stress hormone cortisol in the body was shown to be dramatically lowered after three weeks of eating the prebiotic known as galacto-oligosaccharides.[51]

DISCUSSION

Changes in gut flora may enhance brain health since gut flora impact brain health. It is widely known that the tight connection integrity between enterocytes is supported by the gut flora. Therefore, it shouldn't be surprising that dysbiosis and the resulting elevation in intestinal permeability are now recognised markers of Rheumatoid arthritis, Alzheimer's disease, asthma, Autism spectrum disorders, and other systemic ailments, both inflammatory and non-inflammatory. The processes and functions of the microbiome and probiotics in treating inflammatory disorders, notably IBD, have been thoroughly studied in recent years.[52-57] It is becoming more and more accepted that inflammation plays a role in depression; in addition, anti-inflammatory medications, notably COX-2 inhibitors, have previously proven effectiveness in treating serious depression.[58]

Changes in gut flora may enhance brain health since gut flora impact brain health. The availability of neurotransmitter precursors is decreased and the HPA axis is activated by an inflammatory phenotype, which alters neurotransmitter metabolism and contributes to the pathophysiology of clinical depression.[59,60] It has taken more than a century for convergent aspects of research to establish the gut-brain axis as a crucial gateway to the successful prevention and treatment of clinical depression, despite the fact that it was first proposed in 1910.[61, 62,63]

CONCLUSION

The anatomical and biochemical connections between our gut and brain is termed as Gut- Brain axis. Millions of nerves and neurons run across the gut and the brain. Gut produces neurotransmitters and other chemicals which has a huge impact on the brain.

Various researches have been done to get evidences of gut brain connection and see the impact of this bidirectional relationship in the commencement and progression of various diseases like Rheumatoid arthritis, Alzheimer's disease, Asthma, Autism spectrum disorders, IBD, Depression and other systemic conditions both inflammatory and non-inflammatory. By altering the types of bacteria in your gut, it may be possible to improve thebrain health.Various mood disorders, such as anxiety, depression, and autism spectrum disorders, have well-established linkages to functional GI disruptions.And, altering the gut flora may help our brain function better since gut flora has an impact on brain health.

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