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Psychiatry

FOOD FOR THOUGHT: USE OF DIET TO MODULATE GUT-BRAIN AXIS

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ABSTRACT The Article reviews the anatomical and physiological connections that enable the bidirectional communication between the gut and the brain, identify lifestyle, dietary and microbial influences on the Microbiota-Gut-Brain axis and explore the dietary regimens that can influence mental health and diseases through the Gut and Gastrointestinal Microbiota connections.

KEYWORDS : Diet, Gut, Brain, Psychiatric disorder

INTRODUCTION

Gut Brain axis the two-way biochemical signaling that takes place between the gastrointestinal tract (GI tract) and the central nervous system (CNS) Bidirectional gut–brain interactions regulate key physiological and homeostatic functions, including food intake, immune regulation, and sleep. Alterations in gut brain interactions have long been postulated to play a central role in chronic abdominal pain symptoms and gastrointestinal dysfunction. It consists of the main apparatus as the Gut Microbiom. The term "microbiota" refers to consortia of microorganisms living in a defined environment, while the term "commensals" refers to microorganisms that colonize host without causing a disease (Ref 1). The normal gut microbiota imparts specific function in host nutrient metabolism, drug metabolism, maintenance of structural integrity of the gut mucosal barrier, immunomodulation, and protection against pathogens. The bidirectional communication is done by immune, endocrine, humoral and neural connections between the gastrointestinal tract and the central nervous system (Ref 2). The gut microorganisms influence the function of the brain by releasing the following chemicals: cytokines, neurotransmitters, neuropeptides, chemokines, endocrine messengers and microbial metabolites such as short-chain fatty acids, branched chain amino acids, and peptidoglycans (Ref 3).

The main mechanism of the bidirectional gut-brain axis from gut microbiota to brain – Production, Expression and Turnover of Neurotrasmitters / neurotrophic factor, Protection of intestinal barrier, maintain tight junction integrity, production of bacterial metabolites, maintain mucosal immune regulation and from brain to gut microbiota – it alters mucus, biofilm production, Intestinal Permeability, Immune Function of body.

Gut microbiota can either produce neurotransmitter precursors (including Tyrosine, L-dopa, Tryptophan and 5-hydroxy tryptamine), catalyze the synthesis of neurotransmitters (like Dopamine, Glutamate, GABA, Serotonin, and Norepinephrine) through dietary metabolism. Some bacteria may signal through their metabolites to promote the synthesis and release of neuro transmitters by enteroendocrine cells Neurotransmitters synthesized by bacteria and enteroendocrine cells can enter the blood circulation (Ref 5). Some neurotransmitter precursors can cross the blood–brain barrier and participate in the synthesis cycle of neurotransmitters in the brain. The vagus nerve is classified as 10th cranial nerve and physiologically it is part of parasympathetic system and regulates heart rate, respiration and digestive tract function and have important contribution in neural modulation of immune (Ref 6) system.

The vagus nerve is the major afferent pathway from the abdominal cavity to the brain. It has the key role in gut brain axis transmitting signals from intestinal microbes to the CNS and thus influencing behaviour, mood and development of neurological disorders (Ref 7). Gut can communicate with the brain via hormonal signaling like Ghrelin, Gastrin, Orexin, Cholecystokinin and Leptin and also gut peptide being Neuropeptide Y from entero-endocrine cells can directly act on the brain. Those all are associated with Feeding Behaviour, energy, homeostatis, circadian rhythm arousal and anxiety.

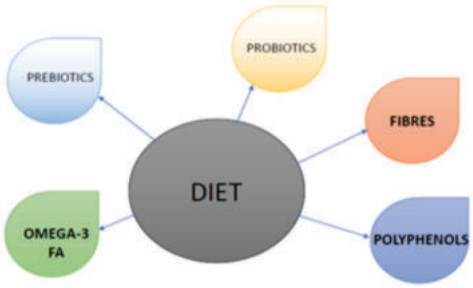

Figure 1: The Dietary Components Affecting the Gut-Brain Axis

The food and its dietary components like Prebiotics, Probiotics, Fibres, Polyphenols, Omega 3 Fatty Acid are found affecting gut brain axis (Ref. 8 & 9). The Indian diet is rich in a variety of whole foods, including vegetables, legumes, and grains, which are high in fiber, antioxidants, and other essential nutrients (Ref 9). As major changes in food seen in now a days and it will correlate to multiple disorders like Chronic Inflammatory Disorders – CVD, Obesity, Depression, Allergies, Diabetes, Autoimmune Disorders. Symbiosis ranges from a commensalistic relationship, wherein the interaction is decided beneficial for one of the partners (the host), to mutualistic, involving beneficial outcomes for all organisms involved. Dysbiosis is an imbalance in bacterial composition, changes in bacterial metabolic activities, or changes in bacterial distribution within the gut. Due to Dysbiosis, overgrowth of pathobionts or reduction of symbionts occur it will lead to leaky gut and altered CNS functions. Possibility of targeting the gut microbiota as treatment for disorders of altered GB interactions (formerly called functional GI disorders) as well as for psychiatric and neurological disorders such as depression, anxiety, Alzheimer's disease, Parkinson's disease, and autism spectrum disorder. Psychological stress and inflammation are common denominators the pathophysiology of diseases in which microbiota may play a role. Stress plays a role in depression, schizophrenia, autism spectrum disorder (ASD), epilepsy, and migraine, whereas inflammation plays a role in depression, schizophrenia, ASD, Parkinson's disease, epilepsy, and migraine.

METHODS:

A literature review was conducted by going through PubMed and Google Scholar databases with the key terms "Gut Brain Axis", "Food", "Diet", "Psychiatric disorders", "Microbiota" and "Mental Helath". Bibliographical and grey literature searches were also performed to obtain the medical curriculum and psychiatry training curricula, including various enrichment activities in psychiatry across the globe. An attempt was made to provide data from all relevant scientific medical journals. Since the focus of the current review is on use of diet to modulate gut-brain axis, the findings have been described narratively.

Findings:

Around eleven research articles focusing on the keywords under study were found from the database. Only those articles which were relevant

& directly associated with the subject under study were included.

Based on various connections and interactions between the Gut & Brain through various pathways it is understood that the Gut has its role to play in various Neurodegenerative conditions like Multiple Scleorosis, Parkinson's Disease, Alzheimer's Disease, Brain Tumors, Ischemic & Hemorrhagic Stroke, as well as Neuropsychiatric conditions like Autism Spectrum Disorder, Depression, Anxiety & Schizophrenia.

The major influences that diet can have seem to be through the alteration & expression of Gut Microbiota activities. Figure 1 shows various mechanisms of bidirectional influence that exists between the Brain & Microbiota. (Ref. 4)

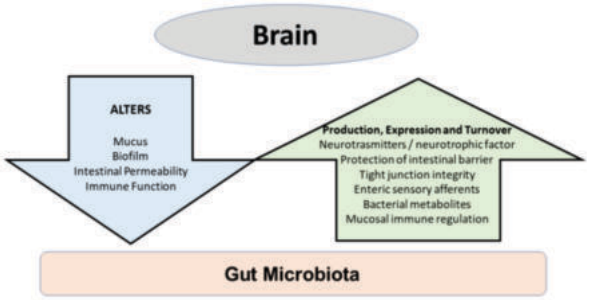

Figure 2: Interactions between Gut Microbiota & Central Nervous System

It is found that 90% of the Serotonin & 80% of Immunity in the body is produced by the Gut. Out of all the factors influencing the Human Gut Microbiota from infancy to old age, diet is the most important factor, with almost 50% changes in Gut Microbiota possible with dietary modifications. The dietary changes have to be done on a regular basis and for a long time to bring about a substantial change. It is well known that food has direct correlation with chronic inflammatory disorders like cerebro-vascular diseases, obesity, depression, allergies, diabetes & autoimmune disorders (Ref 10, 11, 12, 13). It has been found that dysbiosis (overgrowth of pathobionts / reduction of symbionts) leads to leaky gut / chronic inflammation & altered CNS functions. Also, treatment of dysbiosis with diet is found to improve cognitive & behavioural outcomes (Ref 14).

This provides two different modality of intervention: (1) Adding New Microbes Enhancement Preferential Growth Suppression of Undesired ones (2) Preventing Reduction Alteration of Existing Microbial quantity or variety. Considering the variable mediation & modulation first at the gut level & second at the brain level, a plausible model of intervention can work with multiple differing outcomes as shown in Figure 3.

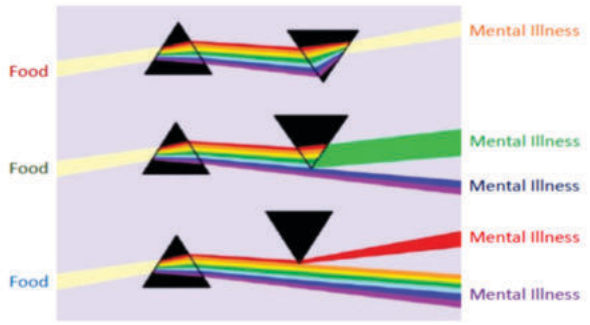

Figure 3: Dietary Interventions: Mediation & Modulation by the Gut & Brain

The following table enlists the human studies establishing the use of Probiotics & Prebiotics as Intervention tool for addressing Mental Health Conditions (Ref. 15-25).

Various studies on rats have shown the effect of Probiotics like Bifidobacteria Longum, Lactobacillus Helveticus, Bacteroides Fragilis, Bifidobacteria Infantis & Lactobacillus Rhamnosus in the form of increased memory / cognition, increased communication, decreased anxiety, decreased pain & depression. Whereas studies on mice / rats to study effects of Prebiotics like high fat diet, high sucrose diet, Mg deficient diet, meat containing diet & western style diet have shown decreased memory & learning, cognitive deficits & anxiety – depressive behaviours (Ref. 15-25).

Among various Probiotic Strains, those with plausible Neuropsychiatric applications can be as follows (Ref: 26-30)

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