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Gut Brain Interaction - A Review

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Abstract

The gut brain axis is a bidirectional system which is highly complex and fragile and is an integral part of the functioning of the human body as it develops the human being. There are various diseases, disorders and factors revolving around this axis and this review looks into said factors. This axis is highly sensitive and is known to play a key role in the development of the brain as well as in the development of disorders such as obesity, depression, diabetes, autoimmune disorders and anxiety among others.The primary component of this axis is the gut microbiota.Its postulated that Gut microbiome can promote and aggravate neurogenerative disorder.Impact of core microbiome on the gene level affects the metabolism. The aim of the study is to analyse the impact made by the studies analysed in this report. 35 articles were taken from various databases and were reviewed for their effect on the topic. This study reviews the articles that discuss the various effects of the gut brain axis. These articles when studied together point at the same fact that there is a lot of potential in this field. This review is an attempt to update recent advancements in Gut-Brain axis, further research is in need of the hour about its complete use to humanity.

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INTRODUCTION

The gut brain axis is a bidirectional and complex system, the interaction is largely due to the effect of this system. The interaction is largely due to the effect of the microbiota present in the gut. This complex has several means of interaction some of which are the neural network between the gut microbiota and the brain, which can, over time, degenerate and result in Parkinson's disease, neuroendocrine-hypothalamic axis gut immune system, intestinal mucosal membrane, neurotransmitters synthesized by gut bacteria, blood brain barrier. This axis is highly sensitive and is known to play a key role in the development of the brain as well as in the development of disorders such as obesity, depression, diabetes, autoimmune disorders and anxiety among others (Westfall *et al.*, 2020). The primary component of this axis is the gut microbiota. Ever since the industrial revolution, the change in lifestyle has resulted in a major change in the diet causing a massive uphaul of bacteria present in the gut, thus each race of the population is going to have different estimates of gut microbiota (Liang *et al.*, 2018).

While it's been observed that men and women have shown different responses to the similar type of situation, altering gut microbiota has an impact on behaviours caused by it affecting the CNS and devel-

opment of body like the tibia, whose ill development may require surgery and certain types of microbiota may appear more frequently than others. This is because microbiota in the gut, not only do they use the host as a carrier, it also performs some functions (Marchesi *et al.*, 2016). They make up to 15% of the brain cells, playing a key role in development of the brain and also have an impact on the blood brain barrier along with a few connection networks such as through foramina even ones that are rarely formed. Exercise has had a positive effect, while being subject to antibiotics can have unfavourable impacts on the body. This shows the importance of the equilibrium between the microbiota and the brain (Duszka and Wahli, 2018). The various diseases and disorders associated with this axis are hypertension, Chronic kidney disease, depression among others.

Over the past years various research was done by our team was on osteology on the importance of posterior condylar canal (Choudhari and Thenmozhi, 2016), accessory foramens present in middle cranial fossa (Hafeez and Thenmozhi, 2016), clinical importance of styloid process (Kannan and Thenmozhi, 2016), Occurance of foramen of Huschke (Keerthana and Thenmozhi, 2016), morphometric analysis of foramen meningo-orbitale (Pratha and Thenmozhi, 2016), Gerdy's tubercle in Tibia (Nandhini *et al.*, 2018), Clinical implication of Occipital emissary formanen (Subashri and Thenmozhi, 2016), stature estimation from facial lengths (Krishna and Babu, 2016), radiation effects of mobile phoneon brain (Sriram *et al.*, 2015), use of i-pads vs textbook in education (Thejeswar and Thenmozhi, 2015), on Mi RNA on hypertension (Johnson *et al.*, 2020), microRNA especially on preeclampsia patients (Sekar *et al.*, 2019), animal studies (Seppan *et al.*, 2018), and in few other fields like thyroid function and obesity (Menon and Thenmozhi, 2016), and vision impairment in amblyopia (Samuel and Thenmozhi, 2015). There is a lack of much information on the current topic of Gut brain interaction hence this research is needed to shed light on the topic and also to measure the impact made by each individual study on the topic at hand. Thus, the aim of the study is to analyse, review various studies on the topic and update the latest research going on the relation between microbiome of gut and brain.

MATERIALS AND METHODS

This research was conceived as scoping literature review. This review has accessed existing reviews and researches in the last decade mostly, through PMC database, MeSH, Google Scholar, Pubmed, Medline, CrossRef and the search terms included were 'gut', 'brain' 'immune system', 'endocrine system', 'development', 'auto immune', 'effect', 'CNS .This review excluded non english researches and retracted articles, The period of duration considered is 1976 to 2020. The total number of articles found on typing the topic is 2,672 and the number of articles actually relevant to the topic is 134, articles were filtered according to the abstract title, complete article and then reviewed. Quality of articles used was assessed using Quality assessment tools and graded as strong, moderate and weak and tabulated (Table 1).

Role of microbiota

Microbiota plays a key role in maintenance of brain health. In a study using rats, changes to gut microbiota can modulate the peripheral nervous system as well as the central nervous system resulting in altered brain function, and diseases which could be prevented by the use of antibiotics and probiotics, in addition to this the importance of the connection between effect on CNS and the body. They have an important impact in the development of the brain. Altering which can lead to disorders, this is because of the equilibrium achieved by the gut and brain through bidirectional communication which exists due to interactions between the two through several links namely neural, endocrine, humoral and immune interactions back and forth between the gut-microbiota and the brain and then from the brain to the gut-microbiota (Carabotti *et al.*, 2015). Impact of core microbiome on the gene level affects the metabolism. In a study involving mice revealed that family members share a similar gut microbiome which is also dependent on the fact that whether the twins are monozygotic or dizygotic. But at the core level, deviations can cause an individual to be obese or lean (Turnbaugh *et al.*, 2009). Improvements to the gut microbiome in turn results in improved skin health with an enhanced resistance to allergens and immune system support and maintenance of human health with pathogenesis of diseases. Some microbiota metabolites like short chain fatty acids affect signalling between gut and brain (Mohajeri *et al.*, 2018). Microbiota Transfer Therapy has resulted in improved ASD (Autism Spectrum Disorder) symptoms by improving symptoms of the gut and in the long run will be more impactful, similar fecal microbiota transplant has been documented to have treated patients with diabetic related diseases. (Kang *et al.*, 2017)

Effect on brain

The microbiota-gut-brain axis is a novel target for the prevention and treatment of neuropsychiatric

Table 1: Quality of study for articles used in review

S. no	Author	Year	Type of study	Key Points	Quality of Study
1	Carabotti *et al.* (2015)	2015	Review	Equilibrium of bidirectional communication results in a healthy development of CNS	Moderate
2	Turnbaugh *et al.* (2009)	2009	Research article	Deviations at core level can cause obesity	Strong
3	Mayer *et al.* (2015)	2015	Research	Factors affecting gut microbiota in utero has impact on brain development	Moderate
4	Kang *et al.* (2017)	2017	Research	Microbiota Transfer therapy improve autism symptoms	Strong
5	Mohajeri *et al.* (2018)	2018	Research	Microbial metabolites affect signalling	Strong
6	Kim and Shin (2018)	2018	Research	GMB axis are a novel target for psychiatric disorders	Weak
7	Spielman *et al.* (2018)	2018	Research	Healthy microbiota has positive neuroimmune response	Moderate
8	Romijn *et al.* (2008)	2008	Review	Axis is involved in many physiological process	moderate
9	Cignarella *et al.* (2018)	2018	Research	Intermittent fasting can lead to inflammatory response	Weak
10	Sun *et al.* (2018)	2018	Research	Reduced expression of TLR4 protects gut brain interaction	Moderate
11	Sylvia and Demas (2018)	2018	Review	Intricate balance affects different behaviours	Moderate
12	Zeeck *et al.* (2018)	2018	Cohort	can aggravate Alzeimer's disease	Moderate

disorders, this is a result of evolutionary association that occurs due to the aforementioned bidirectional communication. Targeting this with probiotics can improve and maybe even prevent neuropsychiatric disorders (Kim and Shin, 2018). The relation between brain and the gut bacteria was established when a study proved that a pathogen free gut made the blood brain barrier decrease in permeability. (Mayer *et al.*, 2015).

For a healthy brain to be present one must always maintain a healthy gut, streptococccal infection can cause neuro inflammation whereas a healthy microbiota in the gut results in a healthy and a positive neuroimmune response (Spielman *et al.*, 2018). A study has found that probiotics resulted in an emotional response being upon administration (Kim and Shin, 2018). Initial colonization of gut microbiota has neurological outcomes due to brain development, dysfunction of microglia can lead to neurode generation and can cause conditions such as obesity, Parkinson's Disease and even Alzheimer's Disease, an intervention into the same can result in the

prevention of said diseases and not fixing the factors affecting gut microbiota can affect brain development and have serious lifelong neurological problem (Mayer *et al.*, 2015).

Development

In Uterobrain development begins in the prenatal stage and any changes can have lifelong impacts in terms of brain development and exposing prenatal infants, but in comparison postnatal exposure to dust and antibiotics in has had less long effects as compared to exposure in prenatal stage, calling for a greater need not to expose prenatal infants to antibiotics to protect them from potential hazard of degenerative diseases in the future (Mayer *et al.*, 2015).

Autoimmune disorder treatment

This can be used for the treatment of disorders such as anxiety and Anorexia nervosa as probiotics can have a therapeutic impact in the treatment of anxiety while there is no medication for the treatment of Anorexia, this disorder causes a rapid change in the gut microbiota which can treated by therapy. Intermittent fasting can have inflammatory effects mediated by gut microbiota, leading to conditions like Multiple Sclerosis and Schizophrenia as alterations to the neurological pathway can lead to neurodegeneration, all these effects are in part modulated by the gut microbiome and intermittent fasting leads to increase in the gut bacteria and can enhance antioxidant pathways (Cignarella *et al.*, 2018).

Effect of foreign substances on the gut.

Intricate balance between gut microbiota if distributed affects each individual differently because these systems do not work alone and work effectively together such that even if one gets affected it also affects the other in a drastic manner (Sylvia and Demas, 2018). Cocoa has been known to cause increased function in the visual cortex of the brain.

Diseases and Disorders

While in earlier studies, it was suggested that there could be a causal relationship between gut microbiota and amyloidosis, it's been proven that TLR4 receptor can cause inflammation and neurodegeneration, the reduced expression of which can ultimately result in improved gut brain axis functioning and less possibility of disorders like autism, Schizophrenia, MDD and several other psychiatric illnesses (Sun *et al.*, 2018). Its postulated that Gut microbiome can promote and aggravate neurogenerative disorder like Alzeimer's disease (Zeeck *et al.*, 2018).

RESULTS AND DISCUSSION

Gut brain interaction was assessed about it's different effects on the body, brain, development of brain, autoimmune disorders, role of microbiota, gut feeling, diseases and disorders Changes in gut microbiota can modulate the peripheral nervous system and the central nervous system altering brain function similar to work of Romjin (Romijn *et al.*, 2008). Obesity being linked at gene level, they found that visceral reflexes influence the CNS and cause obesity. Gut bacteria altercation can be a risk factor for Parkinson's Disease.

CONCLUSION

This study reviews the articles that discuss the various effects of the gut brain axis. These articles when studied together point at the same fact that there is a lot of potential in this field. This review is an attempt to update recent advances in the Gut-Brain axis and its interaction in the body, further research is the need of the hour to know more about its complete use to humanity.

Conflict of interest

The authors declare that they have no conflict of interest for this study.

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