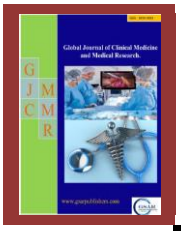

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Microbiota and Mental health: implication for personalized neuropharmacology

By

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Abstract

The gut microbiota is increasingly recognized as a key player in neuropharmacology, influencing drug metabolism, efficacy, and psychiatric treatment outcomes. Dysbiosis, an imbalance in gut microbiota, has been associated with brain disorders such as anxiety, depression and schizophrenia, affecting neurotransmitter systems critical to pharmacotherapy. Personalized neuropharmacology, driven by microbiota profiling, offers a promising avenue for optimizing psychiatric medications. Variability in microbiota composition influences drug absorption, metabolism, and response, highlighting the need for precision medicine in psychiatric treatment. Integrating microbiome analysis into neuropharmacology may enhance drug efficacy, reduce adverse effects, and facilitate targeted interventions using psychobiotics and microbiota-modulating strategies. This review focuses on microbiota's impact on psychiatric pharmacotherapy, examining its role in drug interactions, response variability, and novel therapeutic approaches. Probiotics, dietary modifications, and microbiome-based drug development are explored as emerging strategies for individualized treatment. This review provides a comprehensive analysis of up-to-date findings and future prospects in microbiota-focused pharmacotherapy, paving the way for precision medicine in mental health care.

Key words: *Gut microbiota, Neurodegeneration, Gut-brain axis, Mental health, personalized medicines*

1. Introduction

The microbial flora in the GI tract forms a dynamic ecosystem, marked by significant variability between individuals. Though recent evidence suggests that microbial colonization of the human GI tract starts in the uterus via the placenta, most of the microbiota is acquired from the mother at birth and promptly develop through breastfeeding, dietary intake, and interaction with the environment (García-Mantrana, Bertua et al. 2016), achieving a composition comparable to that of adult life within 2–3 years. Amidst all these pivotal moments, the renowned thousand days shape the basics of our future gut microbiome. As the microbiota composition aims for stability, the relative concentrations of microbial species in the first three years of life fluctuate. These variations permit the developing microbiota to adapt to external factors like the type of breastfeeding (artificial or natural), the potential presence of antibiotics in milk, and continuous dietary changes. By the time a child is three years old, the differences gradually lessen and the groundwork for the future microbiota is created by about 40%. In terms of the represented bacterial species, the remaining 60% of its composition will be impacted by external variables (antibiotics, diet, exercise etc.). In summary, the intestinal microbiota reaches "adult" status in childhood, and about 40% of its composition stays the same throughout life (at least until age 85). In this context, it is crucial to emphasize that the makeup and timing of microbial communities differ significantly from one infant to another, thereby endorsing a more expansive definition of healthy colonization than was previously acknowledged (Palmer, Bik et al. 2007). Other body regions like respiratory tract, vaginal mucosa and the skin also have their unique microbiota, and more recently microbes have been found in areas including the mammary gland, bladder and urethra. The distribution of phyla varies across different body regions. Additionally, dietary habits and geographical location are significant factors that chiefly influence the variation of microbial composition equally between different individuals and within the same individual. It is now acknowledged that approximately one third of the

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microbiota is shared among the human population, whereas the remaining two thirds are unique to each person. Consequently, the microbiota can offer a genuine profile for every individual (Knights, Parfrey et al. 2011). Host and microbiota typically coexist in symbiosis; however, specific conditions or events can promote dysbiosis, which refers to the maladaptation or imbalance of the microbial community, often linked to the emergence of various pathological conditions. Although defining a "healthy microbiota" is challenging, experts generally concur that stability and diversity in its makeup are essential elements promoting optimal health. The composition of the gut microbiota's diversity, stability, and resilience is crucial, and while the significance of stable microbiota states is yet to be completely determined, it is clear that its composition varies over time with the host's physiological condition. The alterations in gut microbiota conditions (linked to medications, inadequate diet, and lifestyle) result in an unhealthy state that could potentially result in diseases. In the GI tract, the majority of the microbiota consists of anaerobic bacteria categorized into 50 bacterial phyla, with the predominant bacterial species grouped into three phyla (98%): the phylum Firmicutes (30–52%), the phylum Bacteroides (9–42%) and the phylum Actinobacteria (1–13%) (Bifidobacterium) (Riaz Rajoka, Shi et al. 2017). Other bacteria, including Escherichia coli (E.coli), Streptococci, and Lactobacilli, exist in minimal quantities (2%). Following an extended period of relative stability that typically defines adulthood, notable alterations in the microbiota composition that arise in later years (Nagpal, Mainali et al. 2018) [10–12] may leads to the onset of neurodegenerative disorders, comprising Parkinson's Disease (PD) and Alzheimer's (AD) which are conditions closely associated with aging. Significantly, while microbiota and its makeup are essential, they are not the sole risk factors for Parkinson's and Alzheimer's disease, which also involve various other elements, including major genetic and neuroinflammatory factors that lead to or contribute to neurodegeneration (Claesson, Cusack et al. 2011). The evidence of the changes in the inflammatory state, noted in Alzheimer's and Parkinson's diseases, intensely suggests the effects of microbiota imbalance, leading to the potential for a mechanistic connection between gastrointestinal dysfunctions and alterations in the brain. Various factors such as diet, inflammatory markers, frailty, cultural and economic contexts, geographic location, and antibiotic therapies contribute to differences in microbiota composition among the elderly (Mariat, Firmesse et al. 2009). Recently, the gut–brain axis has attracted increasing attention due to compelling evidence related to the understanding of novel interactions between the immune, endocrine and nervous systems involving gut microbiota. Consequently, it is not unexpected that a state of dysbiosis has been significantly linked not just with metabolic issues, including obesity and diabetes mellitus or with gastrointestinal disorders, such as IBS (irritable bowel syndrome), IBD (inflammatory bowel disease), and coeliac disease but also with neuropsychiatric conditions (Pascale, Marchesi et al. 2020).

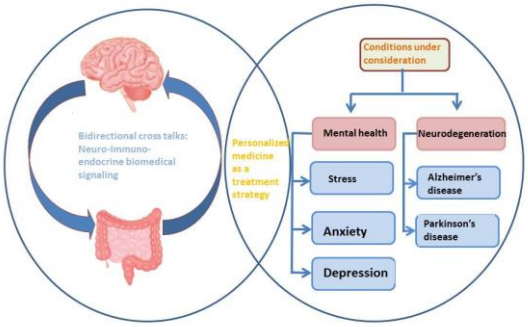

Figure 1: Microbioa and different mental health conditions

2. THE GUT-BRAIN-MICROBIOTA (GBM) AXIS

The primary focus of early studies on the connection between the brain and the gastrointestinal system was on feelings of fullness and digestive processes (Konturek, Konturek et al. 2004). The CNS (central nervous system, as suggested by the brain), the enteric neural system, and the digestive system make up the brain-gut axis. It contributes to the generation of mucus, acid, and bicarbonate as well as hormone secretion and intestinal motility. According to current research, intestinal cells and gut bacteria maintain a symbiotic relationship and are engaged in vital physiological processes such immunological responses, growth, and digesting. Anxiety and other mental health issues associated with stress are closely linked to irritable bowel syndrome (IBS).

This connection has encouraged an examination of the significance of the gut-brain axis. Over 50% of individuals with IBS experience coexisting depression or anxiety (Whitehead, Palsson et al. 2002). The idea that intestinal bacteria affect the brain, behaviour, and stress responses through the microbiota-gut-brain (MGB) axis is supported by recent studies using probiotics, antibiotics, germ-free rodents, , gastrointestinal illnesses, and stool microbial transplants. Through both direct and indirect pathways, gut microbes interact with important parts of the CNS. The endocrine system (hypothalamic-pituitary-adrenal axis), the immunological system (chemokines, cytokines), the autonomic nervous system (efferent and afferent neurones), and the enteric nervous system are all parts of the complex physiological network that includes the MGB axis. By producing bacterial metabolites through tryptophan metabolism, gut microbiota are thought to affect the vagus nerve and the HPA (hypothalamic-pituitary-adrenal) axis (Kim and Shin 2018).

3. Interactions between the Human CNS and Gut Microbiota

3.1. Brain Development and Gut Microbiota

The development of the central nervous system seems to be considerably influenced by gut bacteria. There is evidence that the early activation of the hypothalamic-pituitary-adrenal axis in humans as a stress response is influenced by the gut

*Corresponding Author: **Alina Riaz**

microbiome. The increased stress hormone activation in GF mice is evident of key role of gut bacteria in the development of the HPA axis (Sudo, Chida et al. 2004).

3.2. Evidance of the CNS Influencing Gut Microbiota

The gut microbiome's composition is impacted by both emotional and physical stress. Just two hours of social disruption altered the microbial community's makeup in a mouse model, which led to a decline in the Lactobacillus population. Faecal Lactobacillus levels decreased in rhesus monkeys who suffered from separation anxiety as a result of being separated from their mothers between the ages of 6 and 9 months. In a related study, healthy students who experienced extreme stress had lower levels of Lactobacillus in their faeces than those who experienced mild stress. Stress alters the pattern of mucus release, which can have a negative impact on the development of gut microbes that are fed dietary fibre and prebiotics. After eating, audio stress affects gastrointestinal motility and temporarily reduces stomach emptying in dogs (Rubio and Huang 1992). Mice that experience stress due to mother separation exhibit changes in gut motility and gut microbial composition. Stress mediators can affect the microbial composition through a number of routes and alter intestinal permeability to trigger local immune responses. When adult mice were exposed to chronic stress, the relative abundance of Bacteroides species in the cecum decreased while that of Clostridium species increased. C-C chemokine ligand 2 and Interleukin-6 levels also increased, indicating that the immune system was activated. Because acute stress causes the central nervous system to generate corticotropin-releasing hormone (CRH), which activates mast cells that bind to CRH strongly, intestine and blood-brain permeability improved (Wallon, Yang et al. 2008). Chronic stress further compromised the intestinal barrier by stimulating mast cells, which subsequently permitted microbial metabolites, antibodies, lipopolysaccharides and toxins from the gut to infiltrate the systemic circulation and CNS (Kim and Shin 2018).

3.3. Evidance of Gut Microbiota Influencing the CNS

The cells that cause an infection in the gut microbiota may go to the central nervous system and immediately cause inflammatory reactions. The immune system is impacted by cytokines that enter the bloodstream as a result of persistent low-level inflammation. The chemicals found in the intestinal microbiota have the ability to cause inflammation. For example, two well-known chemicals that cause inflammation are peptidoglycan and LPS. The TLR-4 receptor, which is widely distributed in brain microglia, macrophages, and monocytes, is used to identify LPS. It has been noted that in IBS patients with depression, gut microbiota triggers TLR-4-mediated inflammatory responses (Daulatzai 2014). Changes in blood levels of proinflammatory and anti-inflammatory cytokines can result from the indirect influence of probiotics and gut microorganisms on the innate immune system, which have a direct impact on brain functioning. Proinflammatory cytokine (IFN) expression increased in germ-free animals after E. coli was given to them due to macrophage infiltration and activation in adipose tissue (Kelly, Kennedy et al. 2015).

4. Role of microbiota in different neurological conditions

4.1. Microbiota and Autism (impairment of social behavior)

Animals lacking in microbiota show deficiencies in social behaviour, according to studies conducted on GF mice. In the three-chamber test, John Cryan's research team specifically studied the behaviour of GF mice and discovered that, in contrast to conventionally colonised mice, which spent more time interacting with the new mouse compared to the familiar one, GF mice gave equal amounts of time to both the familiar and novel mice. They found that GF mice engaged with objects or empty spaces more than they did with other mice, which is considered odd behaviour for a social animal. Research has indicated that these behavioural deficiencies can be partially restored by colonising GF mice (Alkhalaf, O'Neill et al. 2014). Oxytocin is widely recognized for its effect on social behavior, and research suggests that the gut microbiota closely regulates its levels (Erdman and Poutahidis 2016). Indeed, Desbonnet et al. (Desbonnet, Clarke et al. 2015) demonstrated that the reduction of gut microbiota starting from early adolescence decreases oxytocin levels in the adult brain. Additionally, a recent study showed that a specific probiotic bacterium (a strain of Lactobacillus reuteri) can adjust oxytocin levels and counteract autism-related behaviors, suggesting the potential to affect social interactions by focusing on gut microbiota. Autism spectrum disorder (ASD) is commonly linked to gastrointestinal co-morbidities, and recent research has indicated alterations in the gut microbiota of autistic children, highlighting shifts in the levels of Firmicutes phyla and Bacteroidetes alongside an increase in Clostridium, thereby reinforcing a significant connection between gut microbiota and ASD (Finegold, Dowd et al. 2010). Research also shows that children with autism have a more diverse microbiome, with Bacteroidetes being significantly more prevalent in severe cases of autism (Finegold, Dowd et al. 2010). Although these associations may not always imply causation, other genera of gut commensals, such as Bifidobacterium, Lactobacillus, Prevotella, and Ruminococcus, have been demonstrated to be altered in autism. Additionally, faecal samples from children with autism have shown a noteable rise in SCFAs, providing more proof that a changed microbiota composition or function plays a role in this neurodevelopmental condition (Wang, Christophersen et al. 2012). However, it is still unknown how SCFAs relate to ASD. While propionic acid infusions into the cerebroventricular region cause autistic-like behaviours in rats, butyrate administration has been shown to reduce repetitive symptoms in a mouse model of ASD, suggesting that SCFAs play different roles in influencing ASD behaviour. As a result, additional research is needed to fully comprehend how SCFAs act in autism. De Theije et al. (De Theije, Wopereis et al. 2014) showed that the autism-like behavioural changes seen in mouse models exposed to valproate correlate with changes in microbiota composition.

*Corresponding Author: **Alina Riaz**

In humans, maternal use of the mood stabiliser valproate during pregnancy is a significant risk factor for autism.

4.2. Microbiota and attention deficit hyperactivity disorder

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition marked by excessive hyperactivity, challenges in behavior regulation, and issues with attention. While Attention deficit hyperactivity disorder is one of the most commonly researched disorders in children and teenagers, the precise mechanisms that make individuals susceptible remain unclear, although it appears that both genetic and environmental influences play a role (Thapar, Cooper et al. 2013). Multiple elements related to the risk of developing ADHD and/or connected to various ADHD symptoms have also been associated with changes in gut microbiota composition, indicating a connection between the microbiota and the condition. Furthermore, data from initial human research indicates that dietary factors affecting gut microbiota may also impact the development or symptoms of ADHD. Consequently, after a recent literature review, Cenit et al contend that ADHD genomic studies ought to incorporate research on gut microbiota (Cenit, Nuevo et al. 2017).

4.3. Microbiota, depression and stress response

Most living things have biological mechanisms that can produce a protective response to threats. The HPA axis is activated in response to stress, and paraventricular neurones in the hypothalamus release CRF (corticosterone-releasing factor). The anterior pituitary secretes adrenocorticotrophic hormone (ACTH) in response to CRF, which in turn stimulates the adrenal cortex to create and release glucocorticoids, such as corticosterone in animals and cortisol in humans.Research involving GF mice has shown that the microbiota affects the maturation of the HPA axis and consequently the response to stress. Animals born and reared in a sterile setting display heightened HPA axis activity, characterized by increased levels of ACTH and corticosterone when faced with a stress (Sudo, Chida et al. 2004). Interestedly, HPA axis function becomes normalized following colonization with commensal bacteria from control mice. While research on the impact of probiotic or prebiotic supplements on human stress behaviors is scarce, it suggests that gut microbiota play a significant role in stress and emotional reactions. Similarly, a probiotic mix (Bifidobacterium longum R0175 and Lactobacillus helveticus R0052) (Messaoudi, Violle et al. 2011) along with a prebiotic (galactooligosaccharide)has demonstrated effectiveness in enhancing the individual's stress resilience and fostering better emotional reactions in healthy individuals (Messaoudi, Violle et al. 2011). Depression is a mood disorder linked to stress that involves a dysfunctional HPA axis, and studies indicate that the gut microbiota significantly influence depression modulation. Indeed, a rise in the alpha diversity of gut microbiota has been noted in those with depression comparing to a healthy control group. Additionally, individuals suffering from depression exhibit notably reduced levels of Lactobacillus and Bifidobacterium in comparison to control participants (Aizawa, Tsuji et al. 2016)[61]. Furthermore, a newer study indicates that individuals with major depression exhibit changes in microbiota compared to healthy individuals, marked by a notable rise in the genera Eggerthella, Gelria, Paraprevotella, Anaerofilm Holdemania and Turicibacter, while reductions in Dialister and Prevotella were noted (Jiang, Ling et al. 2015).

4.4. Gut microbiota and neurodegenerative conditions

More than a hundred years ago, Elie Metchnikoff suggested that gut microbiota affects human health, observing that specific groups who consumed fermented dairy products had longer lifespans. His observations suggested a positive impact of lactic acid bacteria on lifespan. Research later revealed that germ-free mice have a longer lifespan than those with microbiota, indicating a connection between gut bacteria and the aging process. With aging, the composition of gut microbiota shifts, particularly showing a decrease in bifidobacteria and a rise in clostridia, which is linked to health conditions such as frailty. Changes in diet among the elderly may lead to these alterations. Aging similarly diminishes gastrointestinal barrier functionality and affects neuroinflammation, influencing disorders such as Parkinson's disease (PD). Changes in gut microbiota-associated risk factors for PD have been noted, with particular bacterial groups showing significant differences between PD patients and healthy controls. Bacteria that produce butyrate, associated with anti-inflammatory effects, are found in lower numbers in PD patients, whereas pro-inflammatory bacteria are more common. In a similar manner, Alzheimer's disease is linked to changes in gut microbiota and inflammation, affecting cognitive deterioration and the buildup of amyloid plaques. The connection among gut health, metabolic disorders, and neurodegenerative diseases highlights the necessity for more research on dietary approaches and gut microbiota modifications as possible treatments for these issues (Cenit, Sanz et al. 2017).

5. Drug–gut microbiota interactions: implications for neuropharmacology

The microbiome not only changes drug metabolism but can also be influenced by the drug, resulting in either positive or negative impacts on health (Fig. 1). Even with the increasing proof of these interactions, their exact mechanisms remain inadequately understood, requiring additional investigation. Various gut microbiome phyla play crucial roles in its functions, with Firmicutes and Bacteroidetes being the most prevalent (Mariat, Firmesse et al. 2009). The Firmicutes/Bacteroidetes (F/B) ratio frequently reflects bacterial changes, yet it might oversimplify the diversity of human gut microbiota. Elements influencing the composition of gut microbiota throughout the gastrointestinal (GI) tract comprise pH levels, dietary habits, mucus, immune response of the host, and environmental factors. For example, the stomach contains a sparse microbiota in contrast to the large intestine, which is more densely populated. The gut microbiome have an essential part in the nutrient absorption, development of the immune system, protection against

*Corresponding Author: **Alina Riaz**

pathogens and energy balance affecting health and disease management (Björkholm, Bok et al. 2009). The composition of an individual's gut microbiome is influenced by variables like age, gender, ethnicity, lifestyle, diet and environmental factors with newborns' microbiota being particularly affected by the gestational age, method of delivery and feeding practices (Bahr, Tyler et al. 2015). While typically stable in adults, variability rises during illness and at life extremes, such as infancy or old age, rendering these populations more vulnerable to negative drug responses. The increasing acknowledgment of the gut microbiome's impact on drug metabolism has resulted in 'pharmacomicrobiomics', which investigates the microbiome's effect on medications via pharmacokinetics and pharmacodynamics (Matuskova, Anzenbacherova et al. 2014.

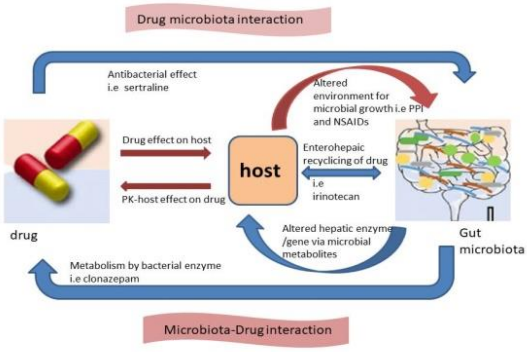

Figure 2: The complex interaction between the gut microbiota and drugs.

The absorption of drugs that are very lipophilic tends to be low, making it imperative to understand microbial influences on drug absorption and metabolism. Gaining better insight into interactions between drugs and human microbiota may domonstrate issues related to drug interactions, as well as explain variation in drug efficacy and adverse reactions in different people. Recent observational studies have revealed significant relationships between gut microbiota composition and various medications. Falony et al. (2016) reported that medication exposure was the primary driver of variation in gut microbiota among participants, with certain drugs such as β-lactam antibiotics and antidepressants being linked to distinct microbial profiles (Falony, Joossens et al. 2016). In the same vein, Zhernakova et al. (2016) showed that some other specific drugs, in particular antibiotics, PPIs, and metformin, tended to alter the composition of gut microbiota, with PPIs strongly altering bacterial pathways (Zhernakova, Kurilshikov et al. 2016). Other groups of medicines, such as anti-inflammatories, gastric acid suppressants, and psychotropic drugs also tend to display different gut microbiota, which calls for further investigation. The effect of drug combinations on microbiota is significant; for example, patients taking a single medication for an extended period exhibit different microbiota profiles than those who do not use drugs. Moreover, the concurrent use of NSAIDs and PPIs changed the composition of certain microbial communities. This new insight highlights the significance of recognizing how drugs may affect microbiota and possibly alter treatment results (Walsh, Griffin et al. 2018).

Table1: The metabolism of drugs by bacterial drug-metabolizing enzymes

Microbiota-derived enzyme	Hypothesized reaction	Drug (or metabolite) substrate	References
β-Glucuronidase	Eliminate glucuronic acid moiety from hepatic phase2 metabolites	NSAIDS, for example, diclofenac and Indomethacin Irinotecan (SN-38 glucuronide)	(Yamamoto, Kurita et al. 2008)
Azoreductase	Reduction of quinone or azo bonds	Ester-containing prodrugs Azo-containing drugs, i.e, olsalazine (5-ASA prodrug) Nitrofurantoin and nitrofurazone	(Ryan 2017)
Carboxylesterase	Hydrolyse amide thioester, carbamate or ester containing drugs to Corresponding free acids Hydrolyse esters to carboxylic Acids	Aspirin, ester-containing prodrugs	(Imai and Ohura 2010)
Nitroreductase	Reduction of nitro group	Benzodiazepines Metronidazole	(Elmer and Remmel 1984)
N-acetyltransferase	Transfer of acetyl group to oxygen or Nitrogen atom of	5-Aminosalicylic acid	(Van Hogezand, Kennis et al.

*Corresponding Author: **Alina Riaz**

	Primary arylamines, hydrazines And N-hydroxylated metabolites		1992)
β-Lyase	Cleavage of C–S bond in hepatic-production cysteine S-conjugate metabolites	Cysteine-conjugated metabolites Bio- activation of sulfur and Seleno cysteine derivatives	(Mikov 1994)
Sulfatases	Hydrolysis of sulfate esters Utilizing for mylglycine	Sulfate ester hepatic metabolites	(Ulmer, Vilén et al. 2014)

6. Significance of microbiota in personalized medicines

The human microbiome impacts the diagnostics and treatment of IBD, diabetes, cirrhosis, and colorectal cancer with an inflammatory focus customizing medicine. Recent research shows relationships between gut bacteria and cancer treatment. Even though information is limited on cancer treatment effects and specific microbiome compositions, mutually exclusive bacterial interactions important for drug effectiveness have been documented. Specific gut microbiome configurations influencing responses to immunotherapy indicate the need to assess drug impact and interactions comprehensively. The gut microbiomes have developed into a biomarker for the disease phenotype, prognosis, and treatment response, especially through changing microbial community structure. F. prausnitzii presence, a beneficial bacterium, correlates with improved postoperative outcomes in Crohn's disease patients. Despite this, the inconsistency in research results on the role of the microbiome in IBD can be attributed to regional differences, antibiotic use, dietary habits, and many of other factors. Consequently, additional research is required to enhance our comprehension of mucosal bacteria in inflammatory diseases such as IBD (Gevers, Kugathasan et al. 2014). Moreover, microbiome patterns have been associated with different gastrointestinal disorders. For instance, F. nucleatum acts as a diagnostic indicator for colorectal cancer, while Clostridium difficile infections correlate with reduced microbial diversity and diminished secondary bile acid production (Rubinstein, Wang et al. 2013). Recent research has even discovered microbial markers that can predict C. difficile infections, with one study showing that patients who underwent fecal microbiota transplantation (FMT) from healthy donors exhibited notable clinical improvement (Jobin 2018). Additional observations emphasize the link between certain microorganisms and treatment outcomes. Patients who respond to anti-PD1 therapy generally exhibit elevated levels of beneficial bacteria like Faecalibacterium, whereas non-responders present higher levels of Bacteroidales. Patients with metastatic melanoma who showed positive treatment responses also exhibited a greater presence of Bifidobacterium longum. The microbial environment plays a crucial role in treatment effectiveness; for instance, antibiotic exposure during cancer treatment may alter the microbial network, weakening the immune response's efficacy (Gopalakrishnan, Spencer et al. 2018). Significantly, comparisons of fecal microbiota indicate that those responding to anti-PD1 therapy exhibit elevated levels of Akkermansia muciniphila in contrast to non-responders. Mice who received FMT from patients with positive treatment outcomes demonstrated greater recovery, which coincided with higher levels of CD8 T cells in the tumors. In contrast, the presence of A. muciniphila in recipients of FMT from non-responders still improved immune cell-mediated antitumor activity. All these findings together illustrate the importance of the microbiome in tailoring individualized treatment plans to enhance therapeutic outcome in cancer care (Sivan, Corrales et al. 2015). Some species of gut microbiota, particularly those belonging to Akkermansia, Faecalibacterium, and Bifidobacterium, have been shown to trigger anti-inflammatory responses, which are crucial for the immune system and preventing overdrive conditions and asserting homeostasis [10]. More importantly, reduced levels of A. muciniphila have been linked with a range of health complications, including inflammatory bowel disease (IBD), type II diabetes, and other allied diseases (Cani and de Vos 2017). Furthermore, F. prausnitzii is known to alleviate intestinal inflammation which is modulated by certain metabolites such as butyrate and salicylic acid originating from host and gut bacteria as well as constituents in peripheral blood (Miquel, Leclerc et al. 2015). These findings underscore the potential therapeutic implications of precision medicine strategies utilizing gut microbiota profile.

Here, the preparatory work of understanding individual microbiotic banners emphasizes the possibility of devising synthetic microbial consortia for the treatment of Clostridium difficile infection (CDI) and inflammatory bowel disease (IBD). The gut microbiota interacts with immune and non-immune cells, having a low or high impact on health through a complex web of metabolites defined as RNAs, DNAs, and membranous constituents. Moreover, the fact that there is a stronger synergy in gut bacteria among patients who respond well to therapies makes this research particularly intriguing. This phenomenon can be explained by the relocation of these bacteria to peripheral lymphoid tissues where specific anti-tumor immune responses are primed. As described, these observations along with other findings show the possibility to consider gut microbiota not only for its role in health moderation but for its potential in treatment enhancement by immune evocation (Behrouzi, Nafari et al. 2019). As so, these

*Corresponding Author: **Alina Riaz**

observations allow the formulation of innovative treatment designs using modifiable gut microbiota to improve the health and the disease state of individuals. The developing understanding around the interplay of gut microbiota and the immune system emphasizes the need for research in this field since it can enhance personalized medicine and create tailored strategies focused on the microbiome.

7. Conclusions and Future Prospects

Our focus is on investigating the gut-brain axis and demonstrating how its component's dysregulation results in mental health disorders and neurodegenerative diseases. Since the microbiota interacts with the brain, lifestyle dicisions are pivotal in ensuring the maintenance of a diverse and balanced microbiota. Consuming a diet rich in sugars and fat could disrupt the balance of the gut microbiota and adversely affect both gut and brain health by altering neurotransmitter metabolism among other pathways. Prebiotics and Probiotics, as noted in some of the previous sections, also contribute to the maintenance of gut health. There is an ongoing study aimed at restoring the microbiota–gut–brain axis on which Akkermansia is being researched as a potential therapeutic agent (Chen, Li et al. 2018, Kalia, Gong et al. 2022). Tailored therapies stand to gain from strategies intended to modify patterns of gut microbiota based on specific parameters or biomarkers. Personalised medicine presents challenges. Disturbances in gut-brain axis components are one of the many contributing aspects that we looked at in this review. Recognising this as a personalised medicine strategy requires looking at the distinctive gut microbiome profiles of patients. In an effort to develop a innovative diagnostic and therapeutic strategy that elucidates the relationship between the gut microbiota and neurodegenerative diseases, scientists have been investigating a variety of sequencing approaches. This encompasses whole-genome shotgun sequencing, multi-omics, 16S rRNA sequencing, metatranscriptomics, metaproteomics and metabolomics (Chen, Li et al. 2018). However, they have a number of shortcomings, such as the intricacy of the data, expense and the trouble of assessing samples with low abundance. Finding new illness biomarkers, analysing the data, and researching potential treatment strategies are still exceedingly challenging tasks. Thus, more technical improvement is necessary to explore the connection between neurodegenerative illnesses and the gut microbiota, which will help develop a meaningful diagnostic and therapy approach. Even though the advancement of these treatments' translational significance in humans remains difficult, they might potentially contribute to a paradigm shift in future therapies.

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