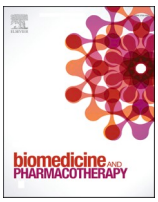
Biomedicine & Pharmacotherapy 156 (2022) 113958

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha



Review

Deciphering the gut microbiome in neurodegenerative diseases and metagenomic approaches for characterization of gut microbes

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ARTICLE INFO

Keywords:
Gut microbiota
Microbiota-gut-brain axis
Metagenomic
Neurodegenerative disease
Bioinformatics

ABSTRACT

The central nervous system has essential role in the regulation of the physiological condition of the human body. Gut microbes cause several types of gastrointestinal diseases like ulcer stomach and intestine and irritable bowel syndrome. Microbes present in the human gut can affect brain function by the release of neuroactive metabolites such as neurotransmitters, hormones, and other compounds. Gut microbial-derived metabolites also have an important role in neurological diseases such as Alzheimer's disease, Parkinson's disease, etc. Vital communication between the gut microbes and the central nervous system is known as the microbiota-gut-brain axis. It provides a communication pathway between the gut and brain which is made up of the vagus nerve, immune system components, and neuroendocrine. Disturbance in gut microbiota composition can alter the central nervous system and enteric nervous system functions. Metagenomics has been employed for the identification, and characterization of gut microbes and microbial-derived metabolites. This review is focused on the gut microbes-brain relationship and the role of gut microbes in neurodegenerative diseases. This study is also focused on major metagenomic approaches and their role in gut microbes characterization.

1. Introduction

The human gut contains diverse microbial species which positively or negatively affect human health [1]. Some microorganisms are essential for the immune system, human digestion, detoxification, nutrition, and human physiology [2]. According to several human gut microbial projects such as the Human Microbiome Project (HMP) and Metagenomics of Human Intestinal Tract (MetaHIT), about 10^{14} microorganisms inhabit the human gastrointestinal tract (GIT) [3]. Bacteria are the most abundant microorganisms of the gut-associated microbial community and they belong to the Kingdom Monera. Balanced compositions of the human GIT microbiota are dominated by Firmicutes and Bacteroidetes phyla. Actinobacteria, Verrucomicrobia, Proteobacteria and Fusobacteria species are also present in the human GIT. Advanced next-generation sequencing (NGS) techniques combined with bioinformatics tools to explore the microbial diversity of gut microorganisms. In the previous study, NGS was potentially used to analyze links between the gut microbiome and human diseases [4]. Mohajeri et al. [5] revealed that Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria are the most numerous microbes in the human GIT, accounting for approximately 64%, 23%, 8%, and 3% of the total microbial population, respectively. Several studies identified that Akkermansiamuciniphila under Verrucomicrobia phyla was also isolated from humans [6]. Host genetic makeup, immune system, and type of nutrition are essential factors to regulate the diversity of the human microbiome [7]. Recently, it has been reported that gut microbes are assumed as essential components showing the interaction with the central nervous system (CNS) and also with the external environmental factor [8]. Gut microbiota interacts with CNS with the help of the vagus nerve, the peripheral nervous system, and the immune system. The communication pathway between CNS and gut microbes is also known as the microbiota-gut-brain axis [9]. Sympathetic and parasympathetic nervous systems (SNS and PNS) are involved in communication pathways between gut microbes [10]. Brain behaviour and physiology are

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https://doi.org/10.1016/j.biopha.2022.113958
Received 16 September 2022; Received in revised form 26 October 2022; Accepted 1 November 2022
Available online 7 November 2022

interdependent on the diversity of gut microbes [11]. The gut microbial community affect the brain's behaviour and physiology [12]. Gut microbes release metabolites which are also involved in several metabolic disorders [13], inflammatory bowel disease [14], neurodegenerative disease and cardiovascular disease [4].

Various studies showed that dysregulation of microbiota-gut-brain axis causes neurological disorders, including Alzheimer's disease, autism spectrum disorder, brain injury, multiple sclerosis, Parkinson's disease and stroke [15–17]. In this review, the authors focused on the correlation between gut microbiota and CNS, and the role of gut microbiota in neurodegenerative disease. This review is also focused on *in silico* metagenomic approaches for gut microbial community analysis. The NGS based metagenomic approaches can play an important role in understanding the causes and mechanisms of neurodegenerative disorders.

2. Human gut microbial communities

A microbiome is known as the whole genomic composition of the microorganisms in a particular niche. Gut microbiota that resides in the gastrointestinal tract provides essential benefits to its host. The alterations of these microbial communities can responsible for immune dysregulation which leads to autoimmune disorders [8]. During homeostasis conditions, the significant role of the microbiome includes defence against the pathogen, inflammation through its interaction with mucosa, synthesis of vitamins, production of energy, modification of dietary elements including fibres, and fatty acids, brain development and its proper function [9]. Microbes of the human gut are also associated with the development and function of the immune system, and gut microbiota also an important role in the permeability of the blood-brain barrier (BBB) [18]. A dysbalance of gut microbiota affects the immune system development, brain function and several other diseases like inflammatory bowel diseases, cardiovascular diseases and cancer [19].

Gut microbiota includes many bacterial populations in GIT symbiotically with the host [20]. The most abundant bacteria are Firmicutes (51%) and Bacteroidetes (48%) including several bacteria such as *Clostridium coccoides*, *Clostridium leptum*, *Lactobacillus genera*, *Bacteroides* and *Prevotella* [21]. The remaining 1% of bacteria belong to the phyla Bifidobacteria, Proteobacteria, Spirochaetes, and Verrucomicrobia [22]. Gut microbiota effectively controls physiological action, including digestion, metabolism and brain functions [23].

2.1. Communication between gut microbes and the nervous system

The enteric nervous system performs as the second brain and provides a relationship with CNS. The microbiota-gut-brain axis is a reciprocal communication pathway in which gut microorganisms interact with CNS [24]. The brain communicates with the intestine via nerves, hormones, and immunological signals [25]. The communication pathways between gut microbes and CNS are shown in Fig. 1.

Microbes enter the bloodstream and produce neuromodulators such as bacteria-derived choline, short-chain fatty acids, host-derived vitamin B_{12} and neurotransmitters like serotonin [26]. Short-chain fatty acids such as butyrate and acetate have an essential role in modifiable brain behaviour with the help of G protein-coupled receptors [19]. Cytokines are produced by the intestinal region's immune cells and reached into the brain via peripheral vessels where cytokines activate the hypothalamic-pituitary-adrenal (HPA). The HPA axis releases cortisol which controls several brain functions [27].

A bidirectional pathway between brain and gut microbes is communicated by the vagus nerve. Back signals from the brain are transmitted to the gut region which controls microbial communities in the human gut [28]. Like motility, secretion of acid, bicarbonates, and mucus; handling of intestinal fluids; and mucosal immune response, all of which are crucial for maintaining the mucus layer and biofilm where specific bacterial groups proliferate in a variety of various microhabitats and metabolic niches connected to the mucosa. By disrupting the typical mucosal environment, a dysregulation of GBA can therefore have an impact on the gut microbiota. Bacterial progeny can also release neurotransmitters such as norepinephrine, serotonin, and dopamine which can interact with the brain and be involved in several brain functions [29]. The microenvironment of the intestinal region can be changed by

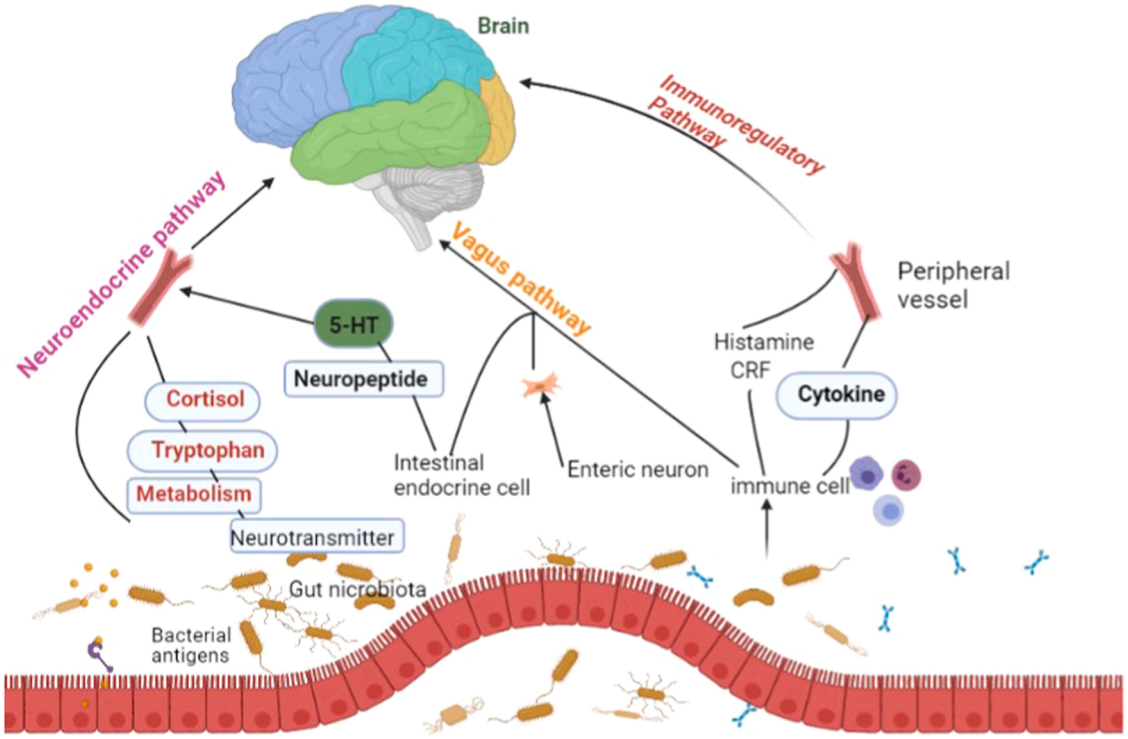

Fig. 1. Correlation between human gut microbes and CNS.

regulating the gut motility, mucosal immunity and secretions of neuronal-glial cells [30]. In addition, gut microbes metabolize to xenobiotics which cause several neurological infections [31].

2.2. Microbial-derived metabolites regulate the function of the human gut

The synthesis of metabolites for preserving the host's metabolic balance and shaping the microbiota-gut-brain axis is an essential function of the gut microbiome [32]. The fatty acids (short-chain fatty acids) are the major microbial-producing metabolites which produce due to the fermentation of dietary fibers in the human gut [33]. Oral consumption of short-chain fatty acids alleviates several metabolic and neurological disorders. Microbes-derived metabolites associated with the host microbiome regulate the immune response, reach the brain through the bloodstream, and modulate neural function [10]. The effectiveness of the gut bacteria in integrating or copying a vast collection of communication particles, such as histamine, γ-aminobutyric acid (GABA), acetylcholine, catecholamines, and serotonin maintenance in changing/monitoring roles of the CNS. *Bifidobacterium infantis* regulates serotonin when rises in the tryptophan level in the blood [34]. Several microorganisms can incorporate and deliver neurotransmitters by changing the status of precursors. There are several examples of metabolites and their producing microbes which involve in neurological function are GABA and norepinephrine produced by *Bifidobacterium* species, *Bacillus* species produce dopamine, *Lactobacillus* secretes acetylcholine, and *Streptococcus and Enterococcus* species produce serotonin [35]. Short-chain fatty acids are involved in microglia homeostasis and brain development as well as the regulation of immunological function [36]. Butyrate is a short-chain fatty acid and product of gut microbiota which have an important role in memory enhancement and synaptic plasticity by inhibiting deacetylation in the histone protein [37]. Butyrate also affects the section of neurotransmitters such as serotonin from enterochromaffin cells of the intestine [25]. Additionally, it has been reported in previous research, propionate produced by gut microbes protects the BBB from oxidative stress [38]. Furthermore, these fatty acids can also influence neuroinflammation by increasing the production and recruitment of components of the immune system such as neutrophils, cytokines and T-cells [39]. SCFAs metabolically regulate T cells and modify the phenotypic of antigen-presenting cells to effectively produce IL-10 + regulatory T cells [40]. When injected into mice, SCFAs can produce CD4 + effector T cells that are highly inflammatory, indicating that the direct action of SCFAs on T cells may potentially be pro-inflammatory in the CNS [41]. Despite their general beneficial effect, SCFAs and their receptors can control autoimmune CNS inflammation both favourably and adversely [40].

3. Characterization methods for gut microbes

3.1. Computational metagenomic approaches

Next-generation sequencing (NGS) has been offered for uncultured microbes, as well as Bioinformatics' rapid advancements [42]. We must identify microbial communities with high sensitivity and specificity before investigating their functional involvement in the pathophysiology of diseases. NGS has dramatically increased these skills by incorporating shotgun and 16 S ribosomal RNA (rRNA) sequencing [43,44]. There are two culture-free approaches to investigating and recognising the gut microbiome including targeted sequencing and shotgun metagenomic sequencing [45]. The major step of the metagenomic study of microbial communities is shown in Fig. 2.

3.1.1. Targeted sequencing

The 16 S rRNA gene is the de facto housekeeping gene in bacterial and archaeal communities [46]. 16 S rRNA sequencing is a well-established, dependable, and reasonably affordable approach for assessing the relative abundance of microorganisms using

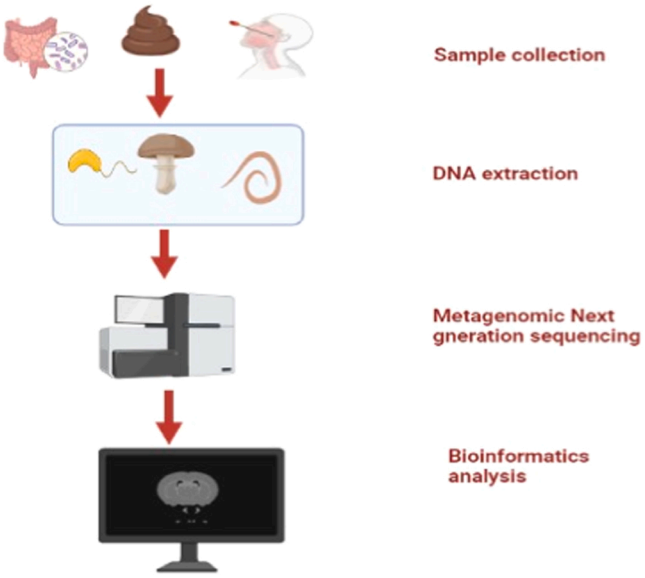

Fig. 2. Metagenomic studies of environmental samples.

next-generation sequencing methods of samples from the gut microbiome of humans, mice, and insects [47]. Targeted sequencing is also termed marker gene sequencing based on 16 S rRNA [48], internal transcribed spacer (ITS), and 18 S rRNA. When the investigation emphasizes the bacteria and archaea in numerous control and patient samples, 16 S ribosomal RNA metagenomics are more feasible and faster to execute in a lab environment. This technique is used to identify the interaction between the gut microbiome, and neurodegenerative disease as shown in Table 1.

This technique uses polymerase chain reaction (PCR) to amplify the

Table 1
16 S rRNA amplicon sequencing to characterize the gut microbiome in the neurodegenerative disease patients sample.

Neurodegenerative diseases	Study	Results	References
PD	PD patients and control.	The altered abundance families of *Bifidobacteriaceae*, *Christensenellaceae*, *Tissierellaceae*, *Lachnospiraceae*, *Lactobacillaceae*, *Pasteurellaceae* and *Verrucomicrobiaceae.*	[49]
AD	C57BL/6 wild-type (WT) and APP/PS1 Tg mice	Environmental noise exposure has harmful effects on the homeostasis of oxi-inflamm-barrier in the microbiome-gut-brain axis.	[50]
HD	Gut microbiome composition of male HD mice and wild-type controls mice at 12 weeks of age.	The researcher investigated the increased abundance of Bacteridetes and decrease of Firmicutes, linked to changes in the gut microenvironment and impaired body weight gain.	[51]
ALS	The faecal microbiota of ALS patients and healthy person	ALS patients do not exhibit substantial changes in the composition of gut microbiota.	[52]

highly conserved genetic sequence [47]. These amplified sequences (amplicons) have been clustered into operational taxonomic units (OTUs) based on their genetic connections, allowing for calculating relative abundance in samples. Methods for defining OTUs include de novo and closed-reference methods [53]. Amplicons have recently been inferred as amplicon sequence variations (ASVs) using several de-noising techniques, such as Deblur and DADA2.

3.1.2. Shotgun metagenomics sequencing

Shotgun metagenomics, while more expensive, provides a larger resolution and accuracy of findings, but they grow more complicated since they contain all microorganisms in a sample, including host DNA [54]. WGS can more correctly describe taxa at the species level and offers more advantages than 16 S rRNA sequencing [44]. WGS increases bacterial diversity detection ranges, improves species identification accuracy, assesses the functional potential of the microbiome, and discovers novel strains or mutations in samples. Shotgun metagenomic sequencing is used to reveal the interaction between gut bacteria and neurodegenerative disease are shown in Table 2.

Both techniques employ a procedure that provides differences throughout studies, specifically through NGS library building for RNA or DNA. We end up with tiny reads (25–500 base pairs) in both approaches, whether we're sequencing a complete sample or 16 S rRNA amplicons, permitting us to identify microbes that are unknown or in small amounts. These reads require substantial bioinformatics pre-processing, including trimming, merging, assembly, scaffolding, and mapping tools [58]. The sequencing process produces unique sequences of the microbial components of the samples reported in fasta or fastq files, as well as a mapping file comprising all of the sample's required metadata. These files will be used as input for the subsequent identification of the species to which the sequences belong and for assigning taxonomy to them [59]. The term "operational taxonomic unit" (OTU) was used to identify groups of identical sequences that might constitute a species are shown in Fig. 3.

Although not perfect, this method generally clusters sequences with a 97% similarity, resulting in selecting one sequence per OTU to represent the taxa it belongs to via phylogenetic alignment. For shotgun and 16 S rRNA metagenomics, several bioinformatics techniques and algorithms exist, either in workflows or in individual implementations of homology- and prediction-based methods.

Table 2
Metagenomic sequencing to characterize the gut microbiome in the neurodegenerative disease patient's sample.

Neurodegenerative diseases	Study	Major results	References
PD	Chinese patients with PD and healthy spouses	*Akkermansia muciniphila* was consistently found to be more abundant in Parkinson's disease patients and decreased abundance of *Prevotellaceae/Prevotella* in Parkinson's disease.	[55]
AD	Nursing home elders	The microbiome of AD individuals has a reduced percentage and frequency of bacteria with the ability to synthesise butyrate and increased abundances of taxa known to induce proinflammatory states.	[56]
HD	Comparison between HD and WT mice.	No significant difference was observed at the phylum level.	[51]
ALS	People with ALS and healthy controls.	The relative abundance of the dominant butyrate-producing bacteria *Eubacterium rectale* and *Roseburia intestinalis* was significantly lower in ALS patients compared to HC.	[57]

3.2. Metatranscriptomics

Morgan and Huttenhower [60] reported bioinformatics and statistical techniques may then be used to discover dysbiosis that may cause disease and possible therapies. However, metagenomics does not give insights into the functional interactions within a complex microbial community or how these interactions may alter in response to an ever-changing environment, such as nutrition [61]. Based on next-generation sequencing, Metatranscriptomics may be utilized to evaluate the expression of genes and the function of microbes directly from microbial assemblages [62]. Chung et al. [63] reported that neurodegenerative disease using metatranscriptomics revealed in Muribaculaceae, genes for carbohydrate metabolism were elevated. In contrast, in Deferribacteraceae, genes for cofactors and vitamin metabolism and amino acid metabolism were upregulated. The major disadvantage of metatranscriptomics is that due to the fast alterations in the mRNA transcript pool, it's uncertain if RNA extracted from faeces may properly represent gastrointestinal activity processes and is not a result of challenging sampling conditions [64].

4. Human gut microbiota and neural diseases

Recent investigation has reported that gut microbiota and their metabolites regulate neural activities and brain function through the microbiota-gut-brain axis [65]. There are several microbial communities present in the human gut. The microbial diversity can be identified through metagenomic approaches. Bacterial identification relied primarily on culture procedures, which frequently failed to identify specific bacteria that do not grow on standard media [66]. This method of bacterial identification is particularly difficult when investigating a community of organisms with varying individual growth characteristics. The current method of choice for characterizing microbial community composition is Next Generation Sequencing. Either 16 S ribosomal RNA gene amplicon sequencing or shotgun analysis of random DNA fragments can be used to determine the taxonomic profile of a microbial population. The 16 S rRNA sequencing technology has provided a simple and successful alternative to microbial cultivation. The 16 S rRNA gene encodes a ribosomal component that is highly conserved among bacteria and has hypervariable areas scattered throughout its sequence [67]. Shotgun metagenomics involves sequencing isolated bacterial DNA from the whole microbial population. Some research reported that shotgun metagenomic identified larger taxa compared to 16 S rRNA sequencing [68]. Gut bacteria is the possible regulating factor in the synthesis of neurological diseases shown in Table 3.

The gut microbiome also significantly modifies brain function, such as the activation of microglia, myelination and neurogenesis. These bacteria also stimulate the mood and behaviour of the host. The function of the gut microbiome in the development of a healthy brain. The establishment and maintenance of the BBB, neurogenesis, myelination, microglial maturation, HPA-axis development, and the HPA-axis response to stress are all crucial processes in the development of the brain. The risk for neurodevelopmental disorders can be considerably raised by any changes to this developing process. Various food components produced from the intestine are required for neuronal cell maturation and correct function in the developing brain [70,71]. Furthermore, new data suggests that gut microorganisms might directly aid in brain development, with long-term ramifications for health [72]. Neuroinflammatory factors such as TNF- α, and IL-6, iNOS are responsible for the pathogenesis of neurodegenerative disease [4].

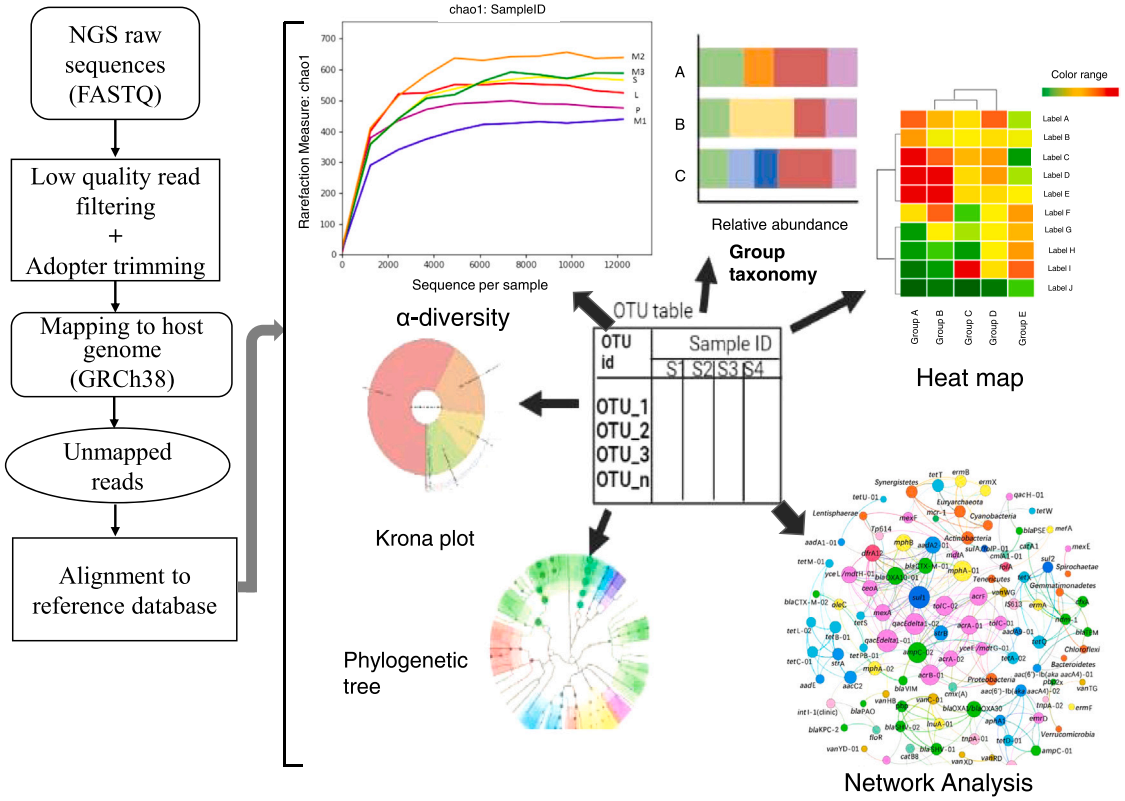

Fig. 3. Using multi-omics approaches show the species diversity of environmental samples.

Table 3
Causes of neurodegenerative disease and Potential therapeutic targets.

Neurodegenerative disease	Gut bacteria dysbiosis	Pathological marker	Potential therapeutic targets	References
Parkinson's disease	Increase *E.coli*, *Ralstonia*, *Oscillospira*, *Bacteroides* and decrease *Prevotellaceae*, *Blautia*, *Roseburia*, and *Cprococcus*.	Increased occurrence of α-synuclein detection, dopaminergic neuronal loss and bowel inflammation.	*Streptococcus salivarius* sub sp thermophilus, *Enterococcus faecium*,	[4]
Alzheimer's disease	Increase of *E.coli*, *Salmonella*, *Klebsiella*, *Bacillussubtillis*, *Staphylococcusaureus*, *Streptomycescoelicolor*.	Increased levels of IL-1β, IL-6, and TNF-α, extracellular amyloids (CsgA, Aβ42, FapC, MccE492) and cerebral deposition	*Lactobacillus* and *bifidobacterium*	[4]
Huntington's disease	*Bacteroidetes, Proteobacteria, Actinobacteria* increases while *Firmicutes, Deferibacteres* decreases	Amplification of CAG (cytosine-adenine-guanine) trinucleotide repeats sequence in the huntingtin gene.		[4]
Amyotrophic lateral sclerosis	Reduction in butyrate-producing microbes (*Butyrivibriofibrisolvens*, *E. coli*, *Oscillibacter*, and *Lachnospira*) and incensement in the microbial population of glucose-metabolizing microbes *Dorea*	Tetanus and botulinum toxins, reduction of butyrate.	Lactobacillus strains	[69]

4.1. Parkinson's disease

Parkinson's disease is another most common neurodegenerative disorder. About 1% of the old age (above 65 years) community is affected by this disorder [73,74]. Numerous researchers confirmed that in this disease patients suffer from non-motor symptoms such as gastrointestinal disease [75]. The aggregation of α-Synuclein in the mucosa and submucosa of the gut, nerve fiber and ganglia is the main neuropathological marker that appeared in Parkinson's disease [76,77]. The α-Synuclein protein of the gut is involved in the communication between the gut and brain via through vagus nerve [78]. The gut microbiome alterations are the most consistent in Parkinson's disease. The increment in bacteria population of genera *Lactobacillus*, *Bifidobacterium* and *Akkermansia*, and decrement in bacterial belong to the genus of *Faecalibacterium*. The common thing in both groups of bacterial communities is producing short-chain fatty acids [79]. This dysbiosis could cause a pro-inflammatory response linked to the patient suffering from recurrent gastrointestinal symptoms.

The beneficial microbes such as *Lactobacillus*, *Bacteroides*, *Prevotella*, and *Bifidobacterium* were reduced in the number of patients suffering from Parkinson's disease. Besides this, the population of pathogenic bacteria such as *Enterobacteria*, *Streptococci*, *Staphylococci*, *Shigella*, and *Helicobacter* was elevated in patients suffering from Parkinson's disease [80]. The gut microbes also have an impact on dopamine production, α-synuclein accumulation, increases oxidative stress, promotes local inflammation, increases intestinal permeability, and causes constipation [81].

Wen et al. [82] reported that using the most recent improved human gut microbiome catalogue, downstream analysis of gut microbial abundance changes between patients and controls allowed for more comprehensive identification of perturbed gut microbial species and strains in Parkinson's disease patients [83]. The anti-inflammatory

action of B. thetaiotaomicron's Pirin-like protein protects epithelial cells via decreasing pro-inflammatory nuclear factor-kB (NF-kB) signalling [84,85].

Borre et al. [85] investigated that Prevotella deficiency was shown in patients, which might be connected to gut microbiota dysfunction and, as a result, contribute to ENS changes. Furthermore, decreased levels of the gut hormone ghrelin, which regulates the function of nigrostriatal dopamine, are related to an increase in Lactobacillaceae and reduce the population of Prevotellaceae in the gut microbiome [86]. The mucin synthesis process in the intestinal layer is regulated by the bacteria *Prevotella*. Thereby, the mucin synthesis in the intestine disturbs the patient suffering from Parkinson's disease.

Additionally, an increase of *A. muciniphila* and a reduction of *Prevotella* bacterial community may lead to mucus degradation and gut permeability. The lack of mucus and increased permeability of the intestinal wall responsible for larger exposure to bacterial endotoxins and other antigenic agents which may be lead to excessive alpha-syn production in the colon and even the brain [87]. Furthermore, the microbiome of Parkinson's disease patients is identified by a reduction in the quantity of butyrate-producing microbes such as *Blautia*, *Coprococcus* and *Roseburia* and a rise in the abundance of proinflammatory Proteobacteria, which may cause inflammation-induced misfolding of alpha-syn [4].

4.2. Alzheimer's disease

It is the most prevalent kind of dementia that affects the elderly, identified as beta-amyloid (Aβ) plaques and neurofibrillary tau tangles which cause intellectual deficiencies, neuroinflammation and memory impairment [88–90]. Neuroinflammation variables such as IL-1β, TNF-α and IL-6 are identified in Alzheimer's disease patients. Previous investigations revealed that amyloid functions as an antimicrobial peptide in the brain [91]. Gut microbiota is considered a dynamic factor for the aetiology of disease due to metabolites derived from microbiota in the cerebral spinal fluid of patients [4]. Several studies have demonstrated the importance of gut microbes in host cognition, and dysbiosis linked to neurodegeneration in old age [5]. Dysbiosis in the gut microbial population causes the production of amyloid as well as lipopolysaccharides (LPS), which disturb the permeability of the gastrointestinal and it also disturbs the function of the BBB [92,93].

Aβ has peptide has antibacterial properties and is part of the innate immune system which protects from pathogenic microorganisms [94]. Additionally, bacterial amyloid exhibits chemical similarity with human Aβ peptide, which causes denaturing and accumulation of Aβ peptide, propagation of the microbiota-gut-brain axis pathway and activation of microglial cells [89]. TLR4 and TLR2 receptors on microglia can detect and remove amyloid compounds. Interestingly, microglial TLR2 release a signal of myeloid differentiation primary response 88 (MyD88) which is responsible for the activation of nuclear factor kappa B and TNF-α. MyD88 also stimulates the production of Aβ by increasing β-secretase and α-secretase. Zhou et al. [95] reported that bacterial-derived amyloids such as prion, tau, α-syn, and prion could act as initiators and assemble with host amyloids in patients suffering from Alzheimer's disease [96,97].

5. Conclusions

In this review, we described the role of gut microbiota on brain function and behavior. We also discuss some computational approaches to analyze the gut microbiota. This review discusses the intrinsic link between gut microbiota and the brain involving various biological processes and how gut microbiota causes pathophysiological changes in the human body and contributes to neurodegenerative disease. New approaches for investigating the microbiome are continuously being created and perfected as technology improves. It is predicted that many multi-omics methods will be developed more shortly, costs will continue to fall, and constraints will be steadily eliminated. This approach may combine many modern technologies to examine the bi-directional connections between neurodegenerative disorders and gut microbiota. Multi-omics analysis of gut microbiota shows the relationship between gut bacteria and the brain. This review used 16 S rRNA sequencing and shotgun metagenomics to characterize the gut microbiota from isolating DNA from faecal samples.

6. Future perspectives

The current study discusses potential of future research directions for determining how human neurodegenerative disease develops and progresses in relation to gut bacteria. The presence of pathogenic bacteria can be determined by comparing the bacterial communities of healthy individuals with patients with diseases. Furthermore, the variations in bacterial community structure could also be used as biomarkers for the detection of neurodegenerative disorders. This studty provide the understanding the interaction of gut microbiota with host immune system and its essential role in the immune dysfunction. It is also provides understanding of change in single gut microbial species affects to host immunity and pathology is challenges.

Funding

The authors would like to acknowledge UGC Dr. D.S. Kothari Postdoctoral scheme for awarding the fellowship to Dr. Sachchida Nand Rai (Ref. No-F.4- 2/2006 (BSR)/BL/19–20/0032).

CRediT authorship contribution statement

Nidhi Singh, Veer Singh and Sachchida Nand Rai: Writing original draft preparation including figures and tables, Conceptualization. **Vishal Mishra:** Reviewing and Editing. **Emanuel Vamanu & Mohan P. Singh:** Supervision, Writing- Reviewing and Editing.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Data availability

No data was used for the research described in the article.

Acknowledgements

The authors are thankful to Centre of Bioinformatics and Centre of Biotechnology, University of Allahabad, Prayagraj, India, for providing internet facilities, working place and instrumentation facilities for this research work.

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