Listen To Your Gut: Exploring Neuronal Dysfunction in the Brain as a Result of Gut Inflammation

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The communication pathway between the gut and the brain has become an area of increased interest with the potential that it has for improvement of overall health. This pathway connecting the gut and the brain is known as the gut-brain axis. The gut-brain axis links the emotional and cognitive aspects of the brain with the intestinal functions within the gastrointestinal tract, creating the bidirectional communication between the central and enteric nervous systems. As a result of the gut involvement within the communication pathway, the gut microbiome has significant influence on the gut-brain axis. Any changes or alterations to the gut microbiome have the potential of also influencing the condition and functions of the brain, leading to potential for utilization of the gut-brain axis in improving human health. With possible changes to the gut microbiome, there comes the common possibility of gut inflammation, which has been linked to the development and progression of neurological disorders such as Parkinson's Disease, Alzheimer's Disease, and Autism Spectrum Disorder, via the vagus nerve. Toll-like receptors (TLRs) play a significant role in the detection of invading pathogens. However, there is a possibility that the activation of TLRs may promote neurodegeneration in such neurological disorders. In this review, we will explore the gut-brain axis in regards to its association with neurodegenerative disorders, as well as factors that may be involved in this communication.

Introduction

The gut-brain axis is a bi-directional communication pathway between the gut and the brain composed of neural pathways throughout the body. This communication between the gut and the brain is well established, with the functional status of the gut being associated with the condition of the brain[1].

The enteric nervous system, a part of the autonomous nervous system, is essential to the functionality of the gut-brain axis, as it is placed at the interface of the gut and the brain[2]. The enteric nervous system innervates the gastrointestinal (GI) tract and is estimated to contain between 400-600 million neurons. The anatomy consists of up to 20 different types of neurons located along the walls of the GI tract, which extends from the esophagus to the anal canal[3]. Although the enteric nervous system receives input from the central nervous system, this system is capable of performing functions on its own, such as propulsion of food, nutrient handling, blood flow regulation, as well as immunological defense. The enteric nervous system has also been associated with the integrity of the epithelial barrier, which plays a significant role in intestinal inflammation and microbial interaction[3]. Even though it is possible for the gut microbiome to communicate through the endocrine and immune pathways in many ways, the vagus nerve pathway is the fastest and the most direct way for the gut to communicate with the brain.

The vagus nerve, a major component of the autonomic nervous system, plays a significant role in maintaining homeostasis within the body through its afferent and efferent pathways. The communication between the gut and the brain through the vagus nerve has been associated with diseases and disorders, including those in mental health, mood regulation, and neurodegeneration[4]. The gut-brain axis plays an important role in the overall communication of the body and as such its implication in the development of neurological disorders is of great interest. Here, we will review the gut-brain axis and its links to neurological diseases.

The Gut Microbiome

The human gastrointestinal tract is the tract of the digestive system that contains a population of microorganisms, which has significant influence on the mental and physical state of the human body[5]. "Microbiota" is the term used to refer to a population of microorganisms that colonize a particular area. Gut microbiota, specifically, is simply used to refer to the microorganisms that are located in the gut. Within the scientific community, there has been significant recent interest regarding gut microbiota and its role in supporting the human body[6]. Gut microbiota provide numerous benefits in maintaining homeostasis in the body, as well as strengthening the gut integrity and regulating immunity[5]. This microbial community primarily consists of prokaryotic species, as well as organisms such as fungi, parasites, and archaea. The term used to refer to the

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genetic and functional profile of the community is known as the gut microbiome. Gut microbial species in a single individual, in total, contain around 3.3 million genes, showing the influence that these species have on the body when compared with the estimate of 23,000 genes in the human genome[7]. With the ongoing investigations of the gut microbiota, there has been growing evidence that the gut microbiota, when in dysbiosis, is associated with the pathogenesis of intestinal and extraintestinal disorders, as well as the development of diseases throughout the human body[8]. Dysbiosis is the loss or gain of bacteria, which either promotes the individual's health or the development of a disease[9].

Each person's gut microbiota is unique in its profile as it has a role in performing specific functions to maintain the ideal state of the gut. The gut bacteria are key participants in regulating digestion along the gastrointestinal tract, in addition to the commensal bacteria playing a significant role in the extraction, synthesis, and absorption of a variety of nutrients and metabolites. The gut microbiota is shaped throughout a human's life depending on factors such as the way the infant was delivered and the methods of milk feeding as well as environmental factors that may have influence on the composition of the gut. As individuals grow older, the composition of their gut changes with the differences in bacterial communities, body mass index level, lifestyle, and cultural and dietary habits, resulting in a unique gut composition for each individual[10]. The gut microbiota continues to increase in its diversity and stability throughout development, but eventually, such growth stops when reaching a certain age. Numerous studies have suggested that the gut microbiome develops into an adult-like configuration by the age of three. The gut microbiome evolves in three different phases: a developmental phase occurring from months 3-14, a transitional phase occurring from months 15-30, and a stable phase beginning from 31 months old, showing that development and functionality of the gut microbiome occurs within the first three years since birth[11]. Even though these studies have suggested that evolution of the gut microbiome occurs until age 3, more recent studies have found that development of the gut microbiome actually may take longer than previously concluded. Recent studies suggest that certain areas of the gut microbiome have already become established by the age of 3, but other areas develop slower, proposing that the gut microbiome may develop slower than originally concluded[11]. This slower development of certain areas of the gut microbiome may be a result of the difference in lifestyles that individuals currently have, which may cause a delay of development of the entire gut microbiome. It is generally known that greater diversity in the gut microbiota is associated with better health outcomes and a lower risk of disorders in the body[7].

Inflammation and the Gut

Inflammation, typically characterized by symptoms, such as redness, swelling, pain, heat and impaired body functions, is the body's defense mechanism when faced with injuries or microbial infections. When the body's immune system senses danger, the process of inflammation is triggered by the cells which are already present in the tissue. During the process, if the cause of inflammation cannot be stopped, the inflammation will continue and become more intense over time in many cases[12]. Inflammation can progress into two categories: acute inflammation and chronic inflammation. Acute inflammation occurs when tissue damage is present as a result of trauma, microbial invasion, or poisonous compounds. This type of inflammation begins rapidly with severe symptoms in a short amount of time, but may only last throughout a short period. Chronic inflammation, on the other hand, is a slow, long-term inflammation that may last for prolonged periods of time. The symptoms that arise with chronic inflammation vary with the extent of the injury and the ability for the body to repair the damage that was caused[13].

Within the gut, there are numerous defense mechanisms in place to protect the immunity of the gut from pathogenic microbes and microbial agents. Although the primary purpose of the GI tract is digestion and absorption of nutrients, bacteria and viruses also have the opportunity to enter the gut. The first line of defense in protecting the gut is the intestinal epithelium, which is a monolayer along the intestines consisting of specialized intestinal epithelial cells[14]. Some of the different subtypes of these specialized intestinal epithelial cells include, absorptive cells, goblet cells, among others, which all contribute to the overall composition of the intestinal epithelium[15]. The intestinal epithelial cells form both physical and chemical barriers to protect the intestinal mucosa from pathogenic microbes. The physical barriers that cover the intestinal mucosa include the mucus layer, which is a layer of viscous fluid secreted by the goblet cells. As a result of the innumerable amount of intestinal bacteria within the large intestine compared to that in the small intestine, the number of goblet cells are also greater in the large intestine, leading to a thicker mucus layer[16]. If pathogenic microbes were to invade the inner mucus layer, the glycocalyx, as well as cell junctions, act as another barrier for the intestinal mucosa. Because the small intestine contains fewer goblet cells compared to the large intestine, the small intestine utilizes chemical barriers for protection, such as antimicrobial peptides and the protein regenerating islet-derived 3. Dysbiosis and impairment of the intestinal epithelial cells have been associated with intestinal inflammation, which may promote the development of various disorders within the body[16].

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Function of Toll-Like Receptors

There are an increasing number of studies that are exploring the composition and metabolic capacity of the gut microbiome of healthy individuals at different stages of their life using the mucosal immune system, which is found throughout the entire GI tract as well as other mucosal surfaces[17]. The gut microbiota interacts with toll-like receptors (TLRs), which are a class of proteins that detect invading pathogens in the innate immune system. TLRs are a distinct class of pattern-recognition receptors localized to the cell surface or intracellular compartments that recognize pathogen-associated molecular patterns, such as lipid, lipoprotein, protein, and nucleic acid. TLRs play a significant role in the innate immune system by signaling through specific adaptor molecules, eventually leading to the activation of transcription factors and innate immune responses. There are 10 members in the TLR family (TLR1-TLR10). TLRs are expressed in innate immune cells and non-immune cells, and are classified by their location: cell surface TLRs and intracellular cell surface TLRs have the primary purpose of recognizing microbial membrane components such as lipids, lipoproteins, and proteins, while intracellular TLRs detect the nucleic acids from bacteria and viruses, as well as self-nucleic acids, such as autoimmunity in disease conditions[18].

TLR2 and TLR4 are two toll-like receptors that play a crucial role in recognizing lipopolysaccharides and peptidoglycans, as well as the production of proteins to protect the immune system from pathogenic bacteria. TLR2, especially, has been found to be associated with genetic inflammatory diseases, which have the possibility of leading to other conditions throughout the body[19]. TLR2 has been known to be one of the most significant toll-like receptors, as a result of its defense against mycobacterial infections, as well as its broad functions in a variety of diseases. TLR2 can bind extracellularly due to it being located on the cell surface, which stimulates the recruitment and interaction between adaptor proteins and the intracellular TIR domain of TLRs, leading to downstream signaling. There has been evidence regarding the benefits of TLR2 signaling when activated to defend against invading pathogens. However, it has also been found that excessive activation of TLR signaling can lead to hyper-inflammation, which has possible associations with chronic inflammatory diseases, autoimmune diseases, as well as the aggravation of infectious diseases. The role that TLR2 plays in the activation and suppression of innate immune responses continues to be unclear. However, it is known that TLR2 plays an important role in innate immunity, despite its inconclusive function in a variety of diseases[20].

Role of the Vagus Nerve In the Gut-Brain Axis

One of the primary roles of the vagus nerve is the maintaining of metabolic homeostasis, as well as the controlling of immune function and proinflammatory responses[21]. The vagus nerve, also known as the tenth cranial nerve, is an important component of the gut-brain axis and the primary nerve of the parasympathetic nervous system, which carries signals throughout the digestive system and its respective organs to the brain, as well as vice versa. Its origin lies in the brainstem, where it extends through the neck and thorax until reaching the abdomen. The vagus nerve plays a crucial role in maintaining the body's homeostasis, as it is responsible for regulating internal organ functions, vasomotor activity, and certain reflex actions[22]. The nerve is considered to be a mixed nerve, consisting of 80% afferent fibres, originating from the mucosa to the muscle layers of the digestive tract, and 20% efferent fibres, originating from the dorsal motor nucleus. The afferent fibres communicate the visceral, somatic, and taste sensations within the body while the efferent fibres release acetylcholine (primary neurotransmitter of the parasympathetic nervous system) through smooth muscles, intrinsic nervous fibres, or secreting cells[23]. Although the left and right vagus nerves develop symmetrically with each other in the beginning, they carry different types of information as individuals grow into adults, with their abdominal and thoracic organs moving into other positions. The left vagus nerve becomes more associated with the ventricles, as it has a lower possibility of causing cardiac effects, while the right vagus nerve becomes more associated with the cardiac atria, resulting in a higher possibility of cardiac effects if stimulated[24].

As well as being a key component of the gut-brain axis, the vagus nerve also plays a significant role in the neuroendocrine-immune axis, which provides a first-line innate defense through neural, behavioral, and endocrine responses against any infections or inflammation, in order to maintain homeostasis[23]. When pathogen-associated and danger-associated molecular patterns are recognized by sensors, such as TLRs, innate immune responses are activated. As a result of the activation, proinflammatory cytokines are released to control inflammation within the body. On most occasions, inflammation is local and temporary, resulting in homeostasis being restored. However, chronic inflammation can occur when the innate immune regulation is disrupted, leading to a continuous release of proinflammatory cytokines. The vagus nerve is an essential part of the inflammatory reflex, a neural reflex mechanism that controls innate immune responses, as well as inflammation[21]. The magnitude of the mechanism is significant, in order to ensure that metabolic homeostasis is achieved, and no other infections or diseases arise as a result. If the inflammatory responses are insufficient, in regards to the extent of the inflammation, they can result in immunodeficiency,

which ultimately can end with infection and cancer. On the other hand, if the inflammatory responses are excessive, they can also cause the emergence of diseases, such as Crohn's disease, Alzheimer's disease, multiple sclerosis, along with many others. Stimulation of the efferent vagus nerve has been associated with the inhibition of the inflammatory response. The vagus nerve, a neural-based anti-inflammatory pathway, contains numerous anti-inflammatory mediators whose primary role is to fight inflammation[25].

Neurological Diseases Associated With The Vagus Nerve

Parkinson's disease

Parkinson's Disease (PD) is a neurodegenerative disease characterized by its progressive neuronal loss in the area of the brain known as the substantia nigra pars compacta, as well as the widespread aggregation of the protein α-synuclein forming Lewy bodies. These Lewy bodies have been found in the substantia nigra and the locus coeruleus, with these areas having the most significant neuronal loss, as well as other areas, such as the cranial nerve nuclei, specifically in the dorsal motor vagal nucleus and the solitary nuclei[26]. The loss of dopaminergic neurons in the substantia nigra leads to dopamine depletion in the body, eventually resulting in the typical motor symptoms of PD, including tremors, slowness of movement, and dizziness[27]. Not only are patients with PD subject to the typical motor symptoms, but such individuals also have almost a sixfold increased risk of developing dementia when compared to those not considered PD patients. Dementia ultimately has a significant influence on morbidity and mortality of PD[28]. The α-synuclein protein has been suspected to form in the enteric nervous system, and spread to the central nervous system through the autonomic nervous system. The vagus nerve has been hypothesized to be a major disease progression route for PD, transporting α-synuclein from the enteric nervous system to the dorsal motor nucleus of the vagus in the lower brainstem[29]. Thus, it is suspected that the protein α-synuclein spreads from the gut to the brain through cell-to-cell transfer. In fact, injection of preformed α-synuclein fibrils into the gut of mice lead to spread of fibrils and neurodegeneration in brain regions involved in PD[30]. There has been evidence showing that aggregation of α-synuclein, which could be due to imbalances in the gut microbiota, causes increased levels of oxidative stress in the gut[31]. This has the possibility of leading to the misfolding and formation of α-synuclein aggregates. The α-synuclein from the gut can reach the brain through systemic and vagal routes. Through the systemic route, gut inflammation may trigger systemic inflammation, ultimately inducing microglia activation. Through the vagal route, the α-synuclein reaches the brain through the vagus nerve, which activates the microglia and worsens neuroinflammation as a result of an increase in oxidative stress[31].

Specifically in Parkinson's Disease, there have been findings of changes in bacteria found in feces of PD patients compared to that of control patients. Several studies found that the majority of the bacteria in the feces of PD and control patients are from the phyla Firmicutes and Bacteroidetes. However, some studies found a significant decrease of Provotellaeae, from the phylum Bacteroidetes, in the feces of PD patients, which could be a possible indicator of PD early on[32].

TLRs have also been found to play a significant role in the neuroinflammation of PD, serving as immune receptors. Studies have been conducted to compare the expression of different TLRs and the TLR-mediated responses between mice models with PD and control groups. It was found from the studies that TLR2, TLR4, and TLR9 had the most influential roles in the pathogenesis of PD, with possible involvement from TLR7 and TLR8. Although there is evidence of the role of TLR involved in PD pathogenesis, it is still unclear of the specific mechanisms of TLRs that contribute to the PD neuroinflammation[33].

Alzheimer's disease

Alzheimer's Disease (AD) is a neurodegenerative disease characterized by disturbances in neuronal circuits of the brain, along with synapse loss, neuronal dysfunction, and neuronal death. This neurodegenerative disorder affects areas of the brain, such as the cerebral cortex and the hippocampus. AD has been associated with the accumulation of the amyloid-β peptide in the brain tissue and cerebrovasculature[34]. Microglia are immunocompetent cells in the brains originating from myeloids, and have been considered to play a crucial role in the development and progression of neuroinflammation, leading to the development of AD. The primary initiator for the activation of microglia in AD is the accumulation of the amyloid-β peptide. The activated microglia activates a mediated inflammatory response, resulting in cell activation and the release of proinflammatory factors. Through this process, the activated microglia eventually lose their phagocytic effect, which leads to the accumulation of the amyloid-β peptide[35].

Similarly to α-synuclein in PD, it has been hypothesized that the release of amyloid from the gut microbiome is the trigger for the misfolding of neuronal proteins, eventually activating neuroinflammation[34]. As individuals age, dysbiosis of the gut microbiome occurs, which has been associated with neurodegeneration. Dysbiosis of the gut microbiome interferes with gastrointestinal permeability and the blood-brain barrier as a result of the secretion of amyloid and lipopolysaccharides[36]. When analyzing the gut microbiome of individuals with AD, it was shown that the microbial richness and di-

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versity has decreased compared to that of an individual without the disease[37]. Through the gut-brain axis, development and progression of AD can be influenced as a result of the alterations within the gut microbiome. Compared with PD, it has been shown that both neurodegenerative diseases have common characteristics, such as the ongoing dementia that is present in patients. Approximately 80% of PD patients eventually develop dementia, which is a primary aspect of AD. Another commonality is the formation of Lewy bodies and α-synuclein, which has been found in over 60% of AD patients[38]. However, there continues to be a lack of certainty if α-synuclein in PD genetically produces the same risk that is found in AD[39].

In Alzheimer's Disease, studies have shown that the composition and the functionality of the gut microbiome can have an effect on the pathology of age-related cognitive impairment and dementia, AD included. A study using 20 kinds of predominant genera models found that there was an abundance of bacteria from the Enterobacteriaceae family, which helped to distinguish the difference between patients with AD and patients with mild cognitive impairment, as well as control patients. This alteration in the gut microbiome could be considered as an implication of AD in patients[40].

Another factor contributing to the pathogenesis of AD is the role of TLRs, specifically TLR4. It is believed to be associated with neuronal damage, production of pro-inflammatory cytokines, blockage of anti-inflammatory pathways, linked to memory loss, along with many others. In one study, lipopolysaccharide (LPS), the archetypal TLR4 agonist, was identified in brain lysates of post-mortem AD brain, with LPS levels being increasingly larger than those from control cases. This has suggested the possibility of LPS contributing to AD through accumulating in the brain from the microbiota[41].

Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a group of heterogeneous neurodevelopmental disorders characterized by social communication deficiency, along with repetitive and stereotyped behaviors. Not only do individuals with ASD have neurological differences, these individuals also have gastrointestinal symptoms, suggesting that the gut microbiome may play a significant role in the pathogenesis of the disorder[42]. It has been shown that individuals with autism have a less diverse gut microbiome, specifically of particular bacteria, such as Prevotella and Coprococcus, carbohydrate degrading and fermenting bacteria[43]. In Autism Spectrum Disorder, there have been multiple studies focusing on the relationship between the gut microbiome and ASD. An increase or decrease in several bacterial families, such as Bacteroidetes, Firmicutes, Proteobacteria, Enterobacteria, Actinobacteria, as well as other phyla, have been found in some studies, possibly being an implication of ASD. However, there are inconsistencies with the studies, as some of them show an increase in a certain bacterial family while others show a decrease or simply no specific pattern at all. These findings have resulted in no conclusions to be made about the connection between the bacteria in the gut microbiome and the ASD[44]. Aside from the differences in the composition of the gut in individuals with autism, increased gut permeability has been an implication of ASD. The impaired intestinal barrier and blood-brain barrier associated with ASD allow bacterial metabolites to cross the intestinal barriers, some of which do not naturally cross the barrier and have the possibility of being neuroactive[43]. These altercations in the gut have led to gut inflammation, which has been linked to the brain inflammation in the central nervous system, with autistic individuals showing active neuro-inflammation in areas of the brain, such as the cerebral cortex, white matter, and cerebellum[45]. In ASD, a dysregulated parasympathetic system and diminished vagal activity have continued to be observed and associated with the disorder[46]. In regards to the role of TLRs within ASD, the activation of TLR4 has continued to be observed, as it has been associated with increased pro-inflammatory cytokines as well as autistic symptoms. However, although there has been speculation on TLRs in the pathogenesis of ASD, more research needs to be done to conclude a clear connection[47]. Although the connection between the gut-brain axis and autism continues to be further researched, there is evidence showing the relationship between gastrointestinal distress and autism, suggesting a physical connection between the gut and the brain[43].

Current Therapies

The stimulation of the vagus nerve has been attempted in order to treat a variety of diseases. Stimulating the left cervical vagus nerve is most commonly done by surgically implanting a pulse generator, for the purpose of minimizing cardiac effects[48]. On the other hand, stimulation of the right cervical vagus nerve is usually done by implanting a programmable device into the right chest, connected to the right cervical vagus nerve. The right cervical vagus nerve is mainly stimulated in the context of heart failure[48]. The vagus nerve has a dual anti-inflammatory role, as a result of the afferent and efferent fibres that it consists of. Vagus nerve stimulation was quite recently approved by the FDA for the treatment of drug-resistant epilepsy and depression. Data provided from Cyberonics in Houston, Texas has shown that around 80,000 patients have been implanted for epilepsy and around 4000 have been implanted for depression. As a result of the implants, it was found that there was a significant reduction in seizure frequency in approximately fifty percent of the patients that participated[23]. The effect that vagus nerve stimulation has on epilepsy and depression is due to the activation of the afferent

fibres of the vagus nerve. Aside from epilepsy and depression, vagus nerve stimulation has also been of interest in the treatment of decreasing long-term inflammation in chronic inflammatory diseases[23]. The anti-inflammatory properties of the vagus nerve from the activation of the afferent and efferent fibres gives more possibilities of stimulating the vagus nerve, in hopes of minimizing symptoms for more diseases. With continuing research, treatments targeting the vagus nerve may be applied to neurological conditions including PD, AD, and ASD.

In Alzheimer's Disease, the amyloid β-protein (Aβ) induces Toll-like receptor 4 (TLR4) activation in microglia, which has prompted researchers to determine if activation of TLR4 could serve as a treatment for AD by regulating neuroinflammation. TLR4 has been found to have significant influence on the pathogenesis of AD, or at least have been closely associated with the occurrence of AD. There have been various methods in targeting TLR4, in regards to therapies for AD, such as flavonoids, medications (Circumdatin D, Resveratrol, bacteria associated with the gut, etc.), specific clinical drugs, as well as others. In targeting TLR4 as therapy for AD, it has concluded in promising results. However, there needs to be more research within the field, in order to fully determine the effectiveness of such methods[49].

Specifically in Parkinson's Disease, there have been many treatments in attempt to either increase or replace dopamine, or prevent the breakdown of dopamine to help stop the pathogenesis of PD or simply help with the symptoms[50]. However, these treatments, such as surgical procedures and medications, have resulted in side effects and overall unsatisfactory results. As a result of the associations between alterations in the composition of the gut microbiota and PD, the gut microbiome has been of interest for the treatment of PD. A variety of studies have found specific alterations to bacterial species in the gut microbiome for those with PD[51]. With this evidence, researchers have attempted to treat PD through the involvement of the gut microbiome. Some methods include attempting to reduce or increase certain bacterial species through antibiotics and probiotics while other methods utilize prebiotics and fecal microbiota transplantation, in order to change the composition of the gut microbiome. Through treatment of the gut microbiome, it may be possible to improve any symptoms or even prevent the pathogenesis of PD[26].

Current Therapies

The gut-brain axis is a major communication pathway connecting the gut to the brain that has been associated with a variety of diseases and disorders. The involvement of the gut microbiome in the communication between the gut and the brain has piqued scientific interest and research has focused on understanding its influence on the body, including in brain health. However, there continues to be little known about the influence that the gut microbiome has on brain health and function, as well as a possibility of using the gut-brain axis as a therapeutic strategy to better brain health and well-being. The association of the gut-brain axis with neurodegenerative diseases opens the door for this communication pathway to be therapeutically targeted to slow or stop the development of the disease and prevent progression to the brain before it becomes irreversible. The composition of your gut changes as you age, along with numerous other factors, such as diet and overall health. It seems many neurodegenerative diseases begin with gut health, and with a deeper understanding, there is potential for targeting and preventing the disease from reaching the brain. The gut-brain axis should continue to be explored so that we may learn more about the role of the gut microbiome throughout the body, as well as factors that may lead to the composition of the microbiome, which all have risk of contributing to the development and progression of brain disorders.

Further research about the connection between the gut-brain axis and neurodegenerative diseases should focus on identifying specific bacterial species that are required for disease progression. Changes in bacterial species have been found in numerous neurodegenerative diseases, supporting the connection between the gut-brain axis and neurodegenerative diseases. If a certain bacterial species is lacking in the gut microbiome, which could be causing the development of a disease, could the bacterial species be added into the gut microbiome to ameliorate disease? Or if a certain bacterial species is overpopulating the gut microbiome, could the bacterial species be taken out of the gut microbiome? Continuing to identify specific bacterial species that may have been altered in the gut microbiome by neurodegenerative disease could help in preventing the development and progression of such diseases reaching the brain. However, the addition of such bacterial species could have significant influence on other aspects of the body as well. It could not be fully determined whether the addition of the absent bacterial species could fully stop the development of the diseases. Microbiota transplantation could be a possible avenue that researchers could take in attempting to stop progression, but such methods could also result in possibly making the disease worse or even produce another disease within the body. Research within the field needs to be continued, in order to conclude potential therapies, but targeting the gut-brain axis could serve as a therapeutic avenue for neurological disorders.

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