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Current role of gut microbiome in Alzheimer's disease

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Abstract. One of the most common forms of dementia is oestrus dementia, which is primarily characterized by cognitive subversion and neural trance. The most obvious pathology is the strong metal disc and neurogenetic fibbers. In recent years, many studies have shown that the intestinal flora in with the change of the AD's development also brings certain effect, play some role. Our bodies are home to many microorganisms, as well as many other fungi (bacteria, fungi, arthritis, and viruses). They can act either as a host or as a neutral or pathological part of the body, taking on both physical and pathological functions. Among them, 95% of microorganisms inhabit the gastrointestinal tract in an intricate ecological colony state, collectively known as the intestinal microbiota. Gut microbiota can affect the blood-brain barrier (BBB) and neurogenesis. If it is more severe, it can lead to neuroinflammation. Sterile study in mice shows that lack of gut microbiota mice increased permeability of blood brain barrier and brain function has changed. Additionally, gut microbiome-targeted therapies, such as GV-971, have shown promise in animal models by modifying gut microbiota composition, reducing neuroinflammation, and improving cognitive function. These findings suggest that modulating the gut microbiome could offer novel therapeutic strategies for AD。 This emphasizes the need for further research in this area to develop effective treatments.

Keywords: Alzheimer's disease, gut microbiome, treatment.

1. Introduction

A neurodegenerative condition that progresses over time is Alzheimer's disease (AD) is most frequently distinguished by the early memory disorders Cognitive decline will eventually have an impact on language, behavior, movement, vision, and spatial orientation. One of the most noticeable cortical atrophies in AD brains is often at least mild, and leaf structure is located on the edge of the multimodal association cortex. Enlarged sulci Spaces with spinal atrophy were frequently observed in frontal and temporal cortex, whereas primary motor and somatosensory cortex were not affected. But so far, no tip has a specific AD symptom [1]. With the introduction of these new criteria, the study of MCI gained popularity in the 2000s. To demonstrate this increased focus and production, Petersen and colleagues (2009) noted that in 1999, fewer than 50 publications were published in the medical literature on the issue of mild cognitive impairment (MCI), whereas by 2007, this number surpassed 900 peer-reviewed studies in that single year (figure 1). Although it can also be observed in other age-related diseases, such as hippocampal sclerosis or silver-loving cereal disease, AD is better known for affecting the amygdala, resulting in the characteristic medial temporal lobe atrophy of the hippocampus, often accompanied by temporal angle dilation. Macroscopic reduction in neuromelanin pigmentation is another common

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feature of AD. The presence of intracellular neurofibrillary tangles and extracellular amyloid plaques, which first appeared more than a century ago, is necessary to diagnose the disease [2]. In the past, Alzheimer's disease could only be diagnosed when plaques and tangles were found by microscopic examination of the brain after death. Now, doctors and researchers can diagnose Alzheimer's disease with more certainty. Biomarkers can identify the presence of plaques and tangles, and expert studies focusing on animal models and humans have shown that gut bacteria closely influence the development and function of the immune system.

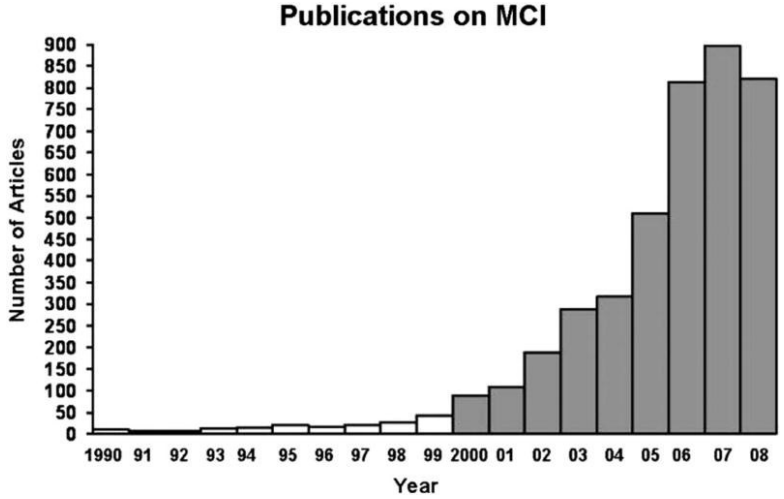

Figure 1. A representative number of publications with the search term “mild cognitive impairment” in the title or abstract from 1990 through part of 2008 [3].

2. The gut microbiome and AD

In the first step, neural stem cells differentiate from the ectoderm during the third week after human conception (after the original gut embryo formation is complete), and these events culminate in the adult brain. The importance of gut microbiota and microbial metabolites in the development of the blood-brain barrier was demonstrated in germ-free mice [4]. In recent years, it has been found that the gut microbiota is closely linked to Alzheimer's disease (AD). The gut microbiota regulates the development of neurons through the microbiome-gut-brain axis, while gut microbiota disorders lead to neurological disorders. Central nervous system dysfunction, chronic inflammation, β-like amyloid β (Aβ) deposition, transmitter imbalance, and oxidative stress caused by intestinal dysbiosis can aggravate the progression of AD. Prebiotics, probiotics, traditional Chinese medicine, fecal transplantation, antibiotics and specific dietary patterns may be potential targets for the prevention and treatment of AD, while Helicobacter pylori infection, chronic noise and aluminum are potential dangers of AD. In the absence of gut microbes, BHS permeates macromolecules more easily than conventionally raised animals. This phenomenon is caused by a decrease in the production of the important tight-linking protein in the cerebral cortex. In addition, permeability was reduced when GF mice were colonized, and vice versa when the short-chain fatty acid butyrate (produced by bacterial fermentation in the gut) was given. The brain barrier and the cerebral lymphatic system are gateways through which the brain receives various signals, such as circulating immune cells and soluble molecules. In both human and mouse models, perinatal antibiotic treatment has been shown to affect the immune status and overall health of offspring. When nonabsorbable antibiotics were given to rodent dams, the gut microbiomes of the mothers and their offspring changed, and the animals became less active than the controls. Additionally, the progeny had conduct resembling anxiety and deficiencies in movement. Similarly, when nonabsorbable antibiotics were given to dams early in gestation, the offspring Wistar rats showed decreased social interaction and increased anxiety [4].

Most importantly, the researchers measured early susceptibility to Alzheimer's disease by the activity of individual neurons, neural networks, and even entire brain regions. The study, which used real

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Alzheimer's patients and laboratory models, highlights how changes in neural susceptibility could potentially be used as biomarkers for early detection of Alzheimer's. Many clinical studies have shown that in patients with familial and sporadic Alzheimer's, the cerebral cortex and hippocampus regions are overactive, and that gut flora can influence Alzheimer's through the central nervous system [5].

3. Mechanisms of action of gut microbiota in driving AD progression

Different species and strains produce gamma-aminobutyric acid (GABA), 5 - hydroxy tryptophan (5 - HT) and histamine and dopamine, these substances as a neurotransmitter or precursor to participate in control of our emotions, our actions and cognitive function. Metabolites are produced by both host and gut microbes during metabolic processes. Metabolites include short-chain fatty acids (SCFAs), which are important for host health. Butyrate, propionate and acetate are the main components of SCFA. They are histone deacetylases or G-protein-coupled receptors. Because these microbial compounds play a positive link between the gut and the brain, they could serve as therapeutic targets for neurodegenerative and developmental diseases. Some immune cells, such as B cells, T cells, macrophages, and dendritic cells, are present in high concentrations in the gut. The gut microbiome can greatly influence the development of organized lymphatic structures and will determine whether to activate the innate and adaptive immune systems. The immune interaction of the gut microbiota with the host leads to the release of pro-inflammatory mediators, such as cytokines and chemokines, and these antibodies are involved in brain immune regulation. In addition, gut microbiota produces metabolites to regulate the maturation, differentiation and activation of microglia and astrocytes in the central nervous system, mediating a variety of neurophysiological processes, including maintaining the integrity of the blood-brain barrier (BBB), neurodevelopment, neurotransmission, and central nervous system immune activation.

4. Gut microbiome-targeted therapies

The central nervous system (CNS) of macrophages is microglia. They are essential for ensuring healthy brain development and homeostasis under normal conditions. In AD, dynamic changes in microglia activation can affect disease progression and play a central role in promoting disease pathogenesis. Microglia can be regulated by gut microbiota. This view is supported by a groundbreaking animal studies, the study reported in GF mice microglia was observed in the overall defects, and no specific pathogens in the antibiotic treatment (SPF) microglia nature serious change was observed in mice, and defective phenotype can be reversed by sharing the experiment part at least 33 it is interesting to note that Two further studies to confirm the effect of intestinal flora g 34, 35, and report the impact time and gender specificity in addition, in the process of aging, driven intestinal flora of intestinal barrier permeability increase lead to enterogenic nf - carboxymethyl lysine to transfer in the brain increases, triggering microglia oxidative stress and mitochondrial dysfunction.

Chimeric antigen receptor (CAR) T-cells and immunotherapy are being tested more and more in frontline and relapsed/refractory tumor settings, mainly in hematologic malignancies (HM). One of the most important host characteristics that may be altered to improve responses to immunotherapy is the gut microbiota. Patients with a more diversified gut microbiome demonstrated a considerably better response and survival rate in several recent human studies undergoing immunotherapy. Based on our understanding of immunology and molecular biology, the question is whether the response to CART cells can be improved if the gut microbiome is targeted to be altered. Several clinical and human studies have shown a link between antigen presentation mechanisms and the diversity of the gut microbiome, and have provided evidence of Treg-inhibiting behavior. Therefore, we hypothesized that the regulation of effective T cells by gut microbiota and Treg homeostasis may influence the behavior of T cell responses. For example, Fraietta et al. proposed a model for predicting CD19+ T cell responses based on T cell basal sets. They found that in LCL patients treated with CD19+ CAR T cells, an increase in IL-6 /STAT3 markers was associated with sustained clinical remission [6].

Signals from the gut microbiota through the gut-brain axis have a major impact on microglia, the resident immune cells of the central nervous system. According to recent research, the gut microbiota

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controls the maturation and function of microglia, which in turn influences how well these cells can modify neurogenesis, synaptic remodeling, and neuroinflammation. The lack of gut microbiota in germ-free animals has been shown to reduce oxidative stress and improve mitochondrial dysfunction in aged brain microglia, indicating the role of the microbiome in age-related alterations in microglial function. Moreover, it has been discovered that the gut microbiota influences how microglial subpopulations change one another, a process that can be successfully stopped by microbial colonization. The complex interactions between microglia and the gut microbiota have important consequences for neurodevelopmental and neurodegenerative diseases.

Starting at 7 months of age, Tg mice were given GV-971 orally in the hope of significantly altering the composition of their gut microbiota within a month. When looking at the altered gut microbiota, treatment with GV-971 in Tg mice significantly reduced Th1 cells in the brain, significantly reduced microglial activation, and reduced levels of various brain cell factors [7]. In addition, the previously observed link between brain lymphocytes and changes in gut bacteria has been disrupted. Simultaneously, GV-971 therapy markedly decreased tau phosphorylation and Aβ plaque deposition, as well as improved the reduction in discriminating learning in Tg mice [8].

5. Conclusion

The complex relationship between the gut microbiome and Alzheimer's disease (AD) highlights the potential for new therapeutic strategies in the pathway: the microbial-gut-brain axis. Studies have shown how gut microbiota affects the development and function of the blood-brain barrier (BHS), neurogenesis, synaptic remodelling, and neuroinflammation. All of these factors are associated with the pathology of AD. The gut microbiota reduces oxidative stress, improves mitochondrial function of microglia, and alters microglia subsets, which are particularly useful during neurodegenerative disease processes. Moreover, gut microbiome-targeted therapies, such as the administration of GV-971, have demonstrated significant benefits in animal models, including altering gut microbiota composition, reducing neuroinflammation, and ameliorating cognitive decline. These findings suggest that interventions aimed at modulating the gut microbiome could offer new avenues for the prevention and treatment of AD, highlighting the importance of further research in this promising field. One of the most important questions is, which gut microbes or short-chain fatty acids are involved in tau pathology? If this problem can be solved, the intervention target for the prevention or treatment of Alzheimer's disease through intestinal bacteria will be found.

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