(REVIEW ARTICLE)

Analysis of the species composition of the intestinal micro biota in stroke patients: Discovering a new risk factors and screening approaches

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Abstract

The human gut contains microbiota, which refers to the collection of microorganisms that inhabit the body. These gut microorganisms can affect the nervous system through the bidirectional communication between the gut and the brain, known as the gut-brain axis. The microbiota can produce various neurotransmitters and signaling molecules that influence the nervous system and the immune system. Alterations in the composition of the gut microbiota, known as dysbiosis, have been associated with neurological disorders such as Parkinson's disease, Alzheimer's disease, and autism spectrum disorders. Maintaining a good and diverse gut microbiota is important for overall health and wellbeing. The composition of the gut microbiota in stroke patients can differ from that of healthy individuals. The emerging evidence suggests that the gut microbiota may play a role in the pathogenesis of stroke and could potentially be a target for therapeutic and preventing interventions. Research is ongoing to fully understand the changes in gut microbiota composition following stroke. Stroke patients have lower levels of beneficial bacterial species, such as Bifidobacterium spp. and Lactobacillus spp., and higher levels of opportunistic bacteria, such as Enterobacteriaceae and Streptococcus spp. The composition of the gut microbiota can differ depending on the type and severity of stroke.

Keywords: Nervous system; Bidirectional communication; Gut-brain axis; Stroke; Gut microbiota composition; Risk factors; Stroke screening

1. Introduction

The microbiota of the gut, or the collection of microorganisms that inhabit the human intestinal tract, have an impact on the nervous system. This is due to the bidirectional communication between the microbiota and the brain, known as the gut-brain axis [1]. The microbiota in the gut can produce various neurotransmitters and other signaling molecules that can influence the nervous system. For example, certain bacteria in the gut can produce gamma-aminobutyric acid (GABA), a neurotransmitter that has been linked to anxiety and depression. Other bacteria can produce serotonin, which is involved in mood regulation and has been implicated in a range of neurological disorders. The microbiota can also influence the immune system, which can in turn impact the nervous system. Certain types of gut bacteria have been associated with an increased risk of autoimmune diseases such as multiple sclerosis, which affect the central nervous system. Moreover, alterations in the composition of the gut microbiota leads to imbalance, a state known as dysbiosis, which have been linked to various neurological disorders, including Parkinson's disease, Alzheimer's disease, and autism spectrum disorders. However, the exact mechanisms by which the microbiota impact the nervous system and contribute to these disorders are still being investigated. Overall, the microbiota can have a significant impact on the nervous system through their influence on the gut-brain axis and immune system. Further research is needed to fully understand the complex interactions between the microbiota and the nervous system and their implications for health and disease. The composition of the gut microbiota can vary widely between individuals and is influenced by factors such as diet, age, genetics, and environment. However, there are some common microbial species that are found in

healthy individuals, which constitute the normal composition of gut microbiota. **Aim** is to find the most common species that form the intestinal microbiome in stroke patients, according to the literature.

2. Overview

The composition of the gut microbiota can vary widely between individuals and is influenced by factors such as diet, age, genetics, and environment. However, there are some common microbial species that are found in healthy individuals, which constitute the normal composition of gut microbiota. The major bacterial phyla found in the gut are *Firmicutes*, *Bacteroidota*, *Actinomycetota*, and *Proteobacteria*. *Bacilliota*, *Firmicutes* and *Bacteroidota* are the most abundant phyla in the gut, representing up to 90% of the total bacterial population. Within these phyla, there are several bacterial genera that are commonly found in healthy individuals. These include *Bifidobacterium spp. (Actynomycetota)*, *Lactobacillus spp. (Bacilliuota)*, *Faecalibacterium spp.*, *Roseburia spp.*, *Ruminococcus spp.*, and *Akkermansia spp*. These bacteria are involved in a range of functions, such as fermenting dietary fiber, producing short-chain fatty acids, and modulating the immune system. Other microorganisms that are present in the gut include fungi, viruses, and archaea. However, these are less well-studied than bacterial species. It is important to note that the composition of gut microbiota can change over time, and imbalances or dysbiosis in the microbiota have been linked to various health conditions. Therefore, maintaining a healthy and diverse gut microbiota is important for overall health and wellbeing. Research has shown that the composition of the gut microbiota in stroke patients can differ from that of healthy individuals. However, there is still ongoing research in this area and more studies are needed to fully understand the changes in gut microbiota composition following stroke. Stroke patients have lower levels of beneficial bacterial species, such as *Bifidobacterium spp.* and *Lactobacillus spp.*, and increased levels of opportunistic bacteria, such as *Enterobacteriaceae* and *Streptococcus spp*. These changes in the gut microbiota may contribute to the inflammatory response that occurs after stroke and exacerbate brain damage. The composition of the gut microbiota can differ depending on the type and severity of stroke. Overall, the research on the gut microbiota composition in stroke patients is still in its early stages, and more studies are needed to confirm and expand upon these findings. Nonetheless, the emerging evidence suggests that the gut microbiota may play a role in the pathogenesis of stroke and could potentially be a target for therapeutic interventions. Here are some studies that have investigated the gut microbiota composition in stroke patients:

The 2021 study aimed to investigate the association between changes in gut microbial composition and the development of hemorrhagic transformation (HT) after stroke. HT was successfully induced in rats injected with glucose and subjected to middle cerebral artery occlusion. Gut microbiota analysis showed an increase in the relative abundance of *Proteobacteria* and *Actinobacteria* in HT rats, and total short-chain fatty acids were significantly lower in HT rats. The study suggests that altered gut microbiota plays a critical role in hyperglycemic HT pathogenesis and susceptibility to HT in stroke rats is associated with inflammation and gut microbiota modulation [2].

The gut microbiota composition and fecal organic acid concentration were evaluated in a Japanese cohort of ischemic stroke patients and age- and sex-matched controls. Ischemic stroke patients showed increased bacterial counts of *Atopobium spp.* cluster and *Lactobacillus ruminis* and decreased numbers of *Lactobacillus sakei* subgroup. Changes in the fecal number of *Lactobacillus ruminis* are positively correlated with serum interleukin-6 levels. Furthermore, ischemic stroke patients had decreased acetic acid concentrations and increased valerian acid concentrations, suggesting that gut dysbiosis in patients with ischemic stroke is associated with altered host metabolism and systemic inflammation [3].

The gut microbiota plays a role in the development of complications in patients with acute ischemic stroke. The study that focuses on the link between the gut microbiota signature and adverse outcomes in stroke patients. Over 500 stroke patients were enrolled, and their clinical data and feces samples were collected to evaluate post-stroke outcomes. The composition of the microbiota was analyzed, and the prognosis and neuropsychiatric complications of patients were tracked. The study provides an opportunity to observe the dynamic changes of the gut microbiota after stroke and contributes to a deeper understanding of risk factors for stroke and the relationship between the gut microbiota and stroke outcomes. The study cohort can be used as a new tool to assess the prognosis of stroke and predict the development of disease [4].

Another article discusses the role of the gut microbiota in stroke and its potential use as a therapeutic target. The gut microbiota has been found to increase the risk of stroke and stroke-induced dysbiosis can contribute to systemic infections. Clinical studies have identified changes in microbial taxa and reduced microbiome diversity in stroke patients. Experimental studies have shown that gut microbiome composition can affect stroke severity and dietary fiber can improve stroke outcome. The article suggests that targeting gut microbiota-derived metabolites could be a new therapeutic approach for stroke prevention and treatment [5].

The study used Mendelian randomization to investigate the causal relationship between gut microbiome and cardiovascular diseases (CVDs). The results showed that genetically predicted genus *Oxalobacter spp.* was positively associated with the risk of coronary artery disease (CAD), while family *Clostridiaceae* was negatively correlated with stroke and ischemic stroke risk. However, there was no causal relationship between other genetically predicted gut microbiome components and CVDs risk. The findings suggest that gut microbiome may have beneficial or adverse causal effects on CVDs risk, providing insights for prevention and management of CVDs [6].

The study used two-sample Mendelian randomization analysis to investigate the causal relationship between gut microbiome and ischemic stroke subtypes. The results showed that specific bacterial features were causally associated with different stroke subtypes. The *Intestinimonas spp.* and the family *Lachnospiraceae*, were found to have a significant protective effect against more than one subtype of ischemic stroke, indicating potential applications of targeted probiotics in stroke prevention [7].

Another article discusses the impact of dysbiosis, or an imbalanced gut microbial community, on stroke recovery and rehabilitation. Using whole genome shotgun sequencing in aged rats of both sexes, the study identified pathogenic bacteria associated with infarct and edema size and inflammatory markers, as well as beneficial bacteria that were decreased following stroke. The findings suggest the need for precision interventions targeting the gut microbiome, such as probiotics that include beneficial bacteria [8].

3. Conclusion

The collection of microorganisms that inhabit the human body, can have a significant impact on the nervous system due to the bidirectional communication between the microbiota and the brain, known as the gut-brain axis. The microbiota in the gut can produce various neurotransmitters and other signaling molecules that can influence the nervous system, and alterations in the composition of the gut microbiota, known as dysbiosis, have been linked to various neurological disorders, including Parkinson's disease, Alzheimer's disease, and autism spectrum disorders. The composition of the gut microbiota can vary widely between individuals and is influenced by factors such as diet, age, genetics, and environment. Maintaining a beneficial and diverse gut microbiota is important for overall health and wellbeing. Emerging evidence suggests that the gut microbiota may play a role in the pathogenesis of stroke and could potentially be a target for therapeutic interventions. Studies have investigated the gut microbiota composition in stroke patients, and alterations in the composition of gut microbiota have been associated with inflammation and neuronal damage in stroke patients. Further research is needed to fully understand the complex interactions between the microbiota and the nervous system as well as their implications in health and disease.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflicts of interest to declare

References

[1] C. Naydenov, T. Manolova, I. Argirova. DYSBIOSIS OR HOW IT CAN RUIN YOUR LIFE THROUGH THE NERVOUS SYSTEM. Trakia Journal of Sciences. 2021; (3):249-252.

[2] Huang, Q, Di, L, Yu, F, et al. Alterations in the gut microbiome with hemorrhagic transformation in experimental stroke. CNS Neurosci Ther. 2022; 28: 77– 91.

[3] Yamashiro K, Kurita N, Urabe T, Hattori N: Role of the Gut Microbiota in Stroke Pathogenesis and Potential Therapeutic Implications. Ann Nutr Metab 2021;77(suppl 2):36-44.

[4] Huijia Xie, Junmei Zhang, Qilu Gu, Qiuyan Yu, Lingzi Xia, Shanshan Yao, Jiaming Liu, Jing Sun, "Cohort Profile: A Prospective Study of Gut Microbiota in Patients with Acute Ischemic Stroke", Advanced Gut & Microbiome Research, vol. 2023, Article ID 3944457, 9 pages, 2023.

[5]   Alex Peh, Joanne A. O'Donnell, Brad R.S. Broughton and Francine Z. Marques. Gut Microbiota and Their Metabolites in Stroke: A Double-Edged Sword. Stroke. 2022;53:1788–1801

[6]   Zhang Y, Zhang X, Chen D, Lu J, Gong Q, Fang J and Jiang J (2022) Causal associations between gut microbiome and cardiovascular disease: A Mendelian randomization study. Front. Cardiovasc. Med. 9:971376.

[7]   Changjiang Meng, MD, Peizhi Deng, MD, Rujia Miao, PhD, Haibo Tang, PhD, Yalan Li, MD, Jie Wang, MD, Jingjing Wu, MD, Wei Wang, MD, Shiqi Liu, MD, Jian Xia, PhD, Yao Lu, PhD, Gut Microbiome and Risk of Ischemic Stroke: A Comprehensive Mendelian Randomization Study, European Journal of Preventive Cardiology, 2023; zwad052,

[8]   Hammond TC, Messmer S, Frank JA, Lukins D, Colwell R, Lin A-L and Pennypacker KR (2022) Gut microbial dysbiosis correlates with stroke severity markers in aged rats. Front. Stroke 1:1026066.