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The relationship between gut microbiota and Parkinson's disease

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Abstract: *The unique environment in the gut and its astounding microbiota creates an ecosystem that is unique to every individual living on this earth. There are more than enough studies done which proofs that the strong neuro-connection between the brain and the gut impact greatly to the daily decisions and motor functions of its host. Previous research has shown a bacterial tyrosine decarboxylase which converts levodopa(used to treat Parkinson's patients) to dopamine can have great impacts on the hosts body. There are also researches that shows that in a germ-free gut microbiota, the model object is less likely to perform symptoms of Parkinson's disease. The question waiting to be solved is: How can we isolate and cultivate healthy gut microbiota to find the key micro-organism that cures Parkinson's disease. By filling in this gap using this research, scientists will be able to advance their way to finding cures for other untreatable disease. Not only will Parkinson's patients benefit from this, many others who might have a critical condition could utilize this new method of medicine.*

Keywords: *Gut flora, gut microbiota, Parkinson's disease, dementia, human microbiota, human microbiome, micro-organisms*

1. Introduction

Although dementia and Parkinson's disease have not been in the historical timeline for a long time, the problem of cure has bothered doctors and researchers for decades. Gut microbiota and Parkinson's has become a heated topic as numerous discoveries proceeds to uncover more about gut microbiota. As time grows, Parkinson's and related diseases seems much more prominent in our communities, unfortunately the disease has impacted too many families. Frankly, with the large number of clinical reports, the effectiveness of treatments vary depending on samples, and the side effects of some treatments cannot be overlooked. Gut microbiota is a complex symbiosis system, and it controls how humans digest and consume. If scientists and researchers can successfully isolate the micro-organisms that contribute greatly towards emotional behavior while maintaining the balance in the existing gut microbiota. Moving forward, they can possibly use a similar technique and find a cure for other complex diseases.

As said before, numerous researchers from different regions across the globe are dedicated in the research between gut microbiota and dementia related diseases such as the Parkinson's disease. For example, researchers at the California Institute of Technology designed and completed an investigation trying to prove this theory. The researchers first bred two groups of rodents that produced too much alpha-synuclein, a protein thought to be one of the "culprits" of Parkinson's disease. The only difference between the two groups was that one group had an intact gut flora and the other was germ-free. It was found that the germ-free rats not only showed no signs of Parkinson's disease, but also performed significantly better on motor tests such as running and pole climbing. The researchers then fed some of the germ-free rats short-chain fatty acids produced by the breakdown of food fibre by gut flora, and transplanted some of the germ-free rats with gut flora obtained from the faeces of Parkinson's patients, and all of them developed Parkinson's disease symptoms. The researchers thus concluded that the gut microbiome is an important driver of Parkinson's disease. Changes in the composition of the gut microbiota or changes in the gut bacteria themselves may contribute to or even cause deterioration in motor function, which is a major symptom of Parkinson's disease. Through this experiment, researchers around the world are able to continue their studies based on the result of the investigation.

Furthermore, Nature published a groundbreaking study on Parkinson's disease in April 2020, claiming that the disease is caused by the aggregation of misfolded proteins known as Lewy bodies. An animal study last year showed that these toxic proteins first accumulate in the intestine and then move up through the vagus nerve to the brain, subsequently causing the death of dopamine-secreting

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neuronal cells in the brain, leading to movement disorders and other common symptoms of Parkinson's disease. The two listed above are just to name a few in the large number of data we have in the relationship between gut bacteria and Parkinson's disease. There is still a lot more to discover and the main problem becomes: how can we use these research to cure Parkinson's.

2. Habits and characteristics of Parkinson's disease

Parkinson's disease is defined as a progressive neurological disorder that affects physical movements in humans. Symptoms can vary based on individuals however tend to follow a similar pattern. They often begin gradually, sometimes with barely noticeable tremors in just one hand. Patients who are affected by Parkinson's disease often experience tremors, bradykinesia, rigid muscles, impaired posture and balance, loss of automatic movements, changes in speech and writing. Tremors are quite common among Parkinson's patients, but the disease also usually causes stiffness or slowed movements.

Based on current research, the core cause of Parkinson's disease is still unknown, however scientists have outlined a few that are likely contributing to the symptoms of Parkinson's disease: genetic mutations, environmental factors. Microscopically, researchers have found that the presence of clumped Lewy bodies holds an important clue to the cause of Parkinson's disease. Due to the fact that the cause of Parkinson's dishes remains a mystery, thus there are no effective ways to fully prevent Parkinson's disease. However, some research has data showing that regular aerobic exercises might reduce the risk of getting Parkinson's disease. The effect of Parkinson's disease should not be overlooked.

Nearly one million people in the U.S. are living with Parkinson's disease, which is more than the combined number of people diagnosed with multiple sclerosis, muscular dystrophy and Lou Gehrig's disease (or Amyotrophic Lateral Sclerosis), and this data is expected to rise to 1.2 million by 2030. Approximately 60,000 Americans are diagnosed with Parkinson's disease each year. More than 10 million people worldwide are living with Parkinson's. The cost to live with Parkinson's is also huge, the combined direct and indirect cost of Parkinson's, including treatment, social security payments and lost income, is estimated to be nearly $52 billion per year in the United States alone. Medications alone cost an average of $2,500 a year and therapeutic surgery can cost up to $100,000 per person. As you can see, we have a huge population and community who are affected by the disease. It is not just the patients were are discussing here, more importantly their families, friends, partners, and so many others who are closely connected with them. The cost has broken too many families and we must find a way to conquer this difficulty. We must call attention to the fact that there are current still no cure for Parkinson's disease, and there has been significant discoveries in hope to find the method to rehabilitate from Parkinson's disease.

3. Previous successes on disease and gut microbiota

The human microbiome comprises of collective genomes of microbiota inhabiting us, namely protozoa, archaea, eukaryotes, viruses and predominantly bacteria that live symbiotically on and within various sites of the human body. In mice, the relationships between host genotype and the gut microbiota have been demonstrated in genetically distinct mouse strains, in which independent quantitative trait loci analysis revealed 169 joint quantitative trait loci intervals that were significantly associated with the abundance of specific microbial taxa in the gut. Scientists including Liping Zhao, Yongde Peng and Chenhong Zhang from Shanghai Jiaotong University said in the latest issue of the American Journal of Science that their trial of groups of diabetic patients found that 89% of patients in the high-fibre diet group were able to regulate their blood sugar levels more effectively, compared to 50% of the control group. The researchers explained that high-fibre foods enrich a group of short-chain fatty acid-producing bacteria in the patients' intestines, which can increase insulin secretion and lead to a significant reduction in glycated haemoglobin. Short-chain fatty acids provide energy for intestinal cells to grow, help the body eliminate inflammation, and increase satiety. Inadequate production of short-chain fatty acids is associated with diseases such as type 2 diabetes.

The new study found that of 141 strains of short-chain fatty acid-producing bacteria, representing the dominant bacteria in the gut, only 15 strains showed a significant increase in numbers following intervention with a high-fibre diet. Genomic analysis showed that these 15 'enriched' strains, belonging to the phyla Thick-walled, Actinomycetes and Aspergillus, possessed more genes to utilize dietary

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fibre, produced more short-chain fatty acids than the other strains and were more tolerant of the acidic intestinal environment.

Feb. 9, 2019 /BIOON/ - Scientists from the University of Toronto and other institutions revealed an association between children with a genetic predisposition to type 1 diabetes and anti-commensal antibodies in their pre-disease serum. According to a study published in the international journal Science Immunology. The researchers conducted an in-depth analysis of whether anti-synthetic antibodies were present in children before the development of autoimmune disease, using the same experiment in which samples were taken from children who carried the HLA gene mutation but did not have type 1 diabetes. The results showed that children with type 1 diabetes and both types of HLA mutation were more likely to have a lower level of response to bacteria than children with HLA mutation but not type 1 diabetes, and the researchers concluded that analysing the body's abnormal immune response may be a way to help predict the likelihood of type 1 diabetes in children with HLA mutation.

This research showed the relationship between gut microbiota and listed a number of micro-organisms that are contributing greatly in hope to keep the host healthy. We must admit that there are thousands more niches that are working in our body in harmony that are yet to be discovered. In contrast, this peaceful harmony can be easily broken by modern medicine, such as excessive antibiotics that are prescribed at an alarming rate, and many other medical procedures that may harm the gut microbiota. There are multiple negative effects, destructions and complications that can happen with the excessive use of antibiotics to the gut microbiota. It can cause an increase in the anti-biotic resistant genes, giving the antibiotic-resistant strains a growth advantage. The strains will then horizontally spread to the microbiomes among bacteria through three kinds of mechanisms: conjugation, transduction, and transformation. Disruption of the gut microbiota by antibiotics can also affect other groups of gut immune cells, manifesting as a dysregulated ratio of type 1 T-helper cells to type 2 T-helper cells, a perturbed differentiation of naive T cells into regulatory T cells, and a reduced frequency of type 17 T-helper cells.

4. Parkinson’s treatments and gut microbiota

Many Parkinson’s disease patients appear to have digestion symptoms before having any classic symptoms of Parkinson’s, for instance constipation. Thus, many patients tend to seek for help in gastroenterology in the early stage, then move onto neurology much later (after the physical inabilities appear). In research published in the journal Nature Communications, scientists at the University of Groningen have found that intestinal bacteria can metabolize levodopa into dopamine. Since dopamine cannot cross the blood-brain barrier, this makes the drug less effective, even though inhibitors exist that would prevent the conversion of levodopa to dopamine. Patients with Parkinson's disease are treated with levodopa, which is converted into dopamine, a neurotransmitter in the brain. In research published in the journal Nature Communications, scientists at the University of Groningen found that intestinal bacteria can metabolize levodopa into dopamine. Since dopamine cannot cross the blood-brain barrier, this makes the drug less effective, even though inhibitors exist that would prevent the conversion of levodopa to dopamine. Levodopa drugs are usually taken orally, and levodopa is absorbed by the small intestine and then transported to the brain via the bloodstream. However, the enzyme decarboxylase converts levodopa into dopamine. In contrast to levodopa, dopamine does not cross the blood-brain barrier, so patients are also given decarboxylase inhibitors. Unfortunately, the level of levodopa reaching the brain varies greatly in Parkinson's disease patients, and we question whether the gut microbiota plays a role in this difference, which makes this investigation strenuous to control. In bacterial samples from the small intestine of rats, researchers discovered the activity of bacterial tyrosine decarboxylase, an enzyme that normally converts tyrosine to tyramine, but also found that the enzyme converts levodopa to dopamine. “We then identified the source of the decarboxylase as Enterococcus." The researchers also found that high concentrations of tyrosine, the main substrate for bacterial tyrosine decarboxylase, did not inhibit the conversion of levodopa. This research reflects how the different enzymes and bacterias in our gut work function mutually, and can greatly impact the patients reaction to medicine. The high diversity in individuals gut microbiota is what makes isolating each bacteria knackering. The researchers also say that they still need to determine which specific bacteria in the gut play an important role in the development of Parkinson's disease before it can become a full-fledged treatment. Mazmanian says that gut flora has a huge physiological role, but at the moment we don't know which bacteria play a role in the development of Parkinson's disease and which bacteria have a protective role. Also, unlike our experiments in mice, there are currently no antibiotic or microbial treatments for humans like we have applied in our experiments in mice. In the near future,

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scientists are aiming to identify specific gut bacteria that have a role in Parkinson's pathogenesis, as this may translate into new biomarkers to identify high-risk patients. In addition, the results of these studies could lead to safer, more effective drugs that avoid complications.

5. Conclusion

In a nutshell, we have discovered the relationship between the Parkinson's disease and the gut flora, but yet we need to find a way to utilize the micro-organisms living in the gut. If we are able to isolate and develop a sterile environment that mimics the human gut, then creating the solution for many convoluted diseases will become apparent. These contemporary treatments will be much more efficient and accessible to the patient since we will be able to harvest the micro-organisms easily, with no side-effects. As many may say, the gut microbiota is a key to a brand new area of neuroscience in sanguine to save millions of lives.

References

[1] Van Kessel , S. P., El Aidy, S., van Dijk, G., Keshavarzian, A., Castejon, M., El-Gendy, A. O., & Frye, A. K. (2019, January 18). Gut bacterial tyrosine decarboxylases restrict levels of levodopa in the treatment of parkinson's disease. PubMed.org.https://pubmed.ncbi.nlm.nih.gov/30659181/.

[2] Aho, V. T. E., Pereira, P. A. B., Voutilainen, S., Paulin, L., Pekkonen, E., Auvinen, P., & Scheperjans, F. (2019, June 18). Gut microbiota in parkinson's disease: Temporal stability and relations to disease progression. EBioMedicine.https://www.sciencedirect.com/science/article/pii/S235239641930372X.

[3] Durack, J., & Lynch, S. V. (2019, January 7). The gut microbiome: Relationships with disease and opportunities for therapy. The Journal of experimental medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6314516/#bib203.

[4] Mayo Foundation for Medical Education and Research. (2020, December 8). Parkinson's disease. Mayo Clinic.https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/symptoms-causes/syc-20376055.

[5] Paun, A., Yau, C., Meshkibaf, S., Daigneault, M. C., Marandi, L., Mortin-Toth, S., Bar-Or, A., Allen-Vercoe, E., Poussier, P., & Danska, J. S. (2019, February 1). Association of HLA-dependent ISLET autoimmunity with systemic antibody responses to Intestinal commensal bacteria in children. Science Immunology. https://immunology.sciencemag.org/content/4/32/eaau8125.

[6] Romano, S., Savva, G. M., Bedarf, J. R., Charles, I. G., Hildebrand, F., & Narbad, A. (2021, March 10). Meta-analysis of the parkinson's disease gut microbiome suggests alterations linked to intestinal inflammation. Nature News. https://www.nature.com/articles/s41531-021-00156-z.

[7] Sampson, T. R., Debelius, J. W., Thron, T., Janssen, S., Shastri, G. G., Ilhan, Z. E., Challis, C., Schretter, C. E., Rocha, S., Gradinaru, V., Chesselet, M.-F., Keshavarzian, A., Shannon, K. M., Krajmalnik-Brown, R., Wittung-Stafshede, P., Knight, R., & Mazmanian, S. K. (2016, December 1). Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease. Cell.com.https://www.cell.com/cell/fulltext/S0092-8674(16)31590-2?_returnURL=http%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867416315902%3Fshowall%3Dtrue.

[8] Shen, T., Yue, Y., He, T., Huang, C., Qu, B., Lv, W., & Lai, H.-Y. (1AD, January 1). The Association between the gut microbiota and Parkinson's disease, a meta-analysis. Frontiers. https://www.frontiersin.org/articles/10.3389/fnagi.2021.636545/full.

[9] Statistics. Parkinson's Foundation. (n.d.). https://www.parkinson.org/Understanding-Parkinsons/Statistics.

[10] Thomas, L. (2020, May 22). Gut bacteria Affecting parkinson's Treatment. News-medical. https://www.news-medical.net/health/Gut-Bacteria-Affecting-Parkinsone28099s-Treatment.aspx.

[11] Wexler, M. (2021, March 15). Bacteria in patients' guts show changes that may weigh on disease. Parkinson's News Today. https://parkinsonsnewstoday.com/2021/03/15/parkinsons-microbiome-gut-bacteria-differs-may-affect-disease/.

[12] Zhang, S., & Chen, D.-C. (2019, May 20). Facing a new challenge: The adverse effects of antibiotics on gut microbiota and host immunity. Chinese medical journal. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6511407/.

[13] Xinhuanet.(2018, March 10).Chinese scientists have found the gut bacterial groups that can help treat diabetes.Chinese scientists have found that the intestinal bacterial flora that can help treat diabetes-Xinhuanet.http://www.xinhuanet.com/tech/2018-03/10/c_1122516829.htm.