ISSN 2350-109X
www.indianscholar.co.in

Indian Scholar

An International Multidisciplinary Research e-Journal

INVESTIGATION ON THE LINK BETWEEN GENETICS AND PARKINSON'S DISEASE

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Abstract

Many scientists have researched day and night to prove that Parkinson's disease is a hereditary disease but have been unsuccessful. However, there are many different forms that have shown Parkinson's disease to be established in patients with relatively rare type of Parkinson's; this is the monogenic form of Parkinson's disease. This research paper covers the main genes that affect Parkinson's disease, why and how gene mutations affect Parkinson's and statistics related to the same.Familial Parkinsonism has been seen to be established when there are certain mutations in 5 specific genes that are taken into consideration in this research paper. Those 5 include SNCA, PARK2, DJ-1/PARK7, PINK1, LAARK2. However, functions of these genes and their mutations leading to Parkinson still remain to be fully elucidated.

Keywords:*SNCA, PARK2, DJ-1/PARK7, PINK1, LAARK2, Mutation, Hereditary*.

INTRODUCTION

The domain that this research paper comes under is "Bioinformatics and scientific computing".Bioinformatics aims to include representing data, communication of data, and in the end processing of data. Analysis can be done by the use of informatics. Bioinformatics together means studying and representing the biological analytical data to give the required output. This research paper is aims to understand the current scenario based on Parkinson's disease and its relation with genetics; Investigations that have taken place for the same have also been taken into consideration. Parkinson's disease is one of themost common diseases which includes nerves and neurons just after Alzheimer's disease. Parkinson's disease is a brain disorder that makes the body vibrate or shake in its own way without any control of the human being. Basically, the body now becomes involuntary in movement. The causes for this disease are when the neurons in the brain that control movement gets impaired or die. This results in dopamine reduction which intake causes all types of moving disorders. Moreover, the nerve endings that produce norepinephrine (a chemical messenger) are also lost.

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Theory

When considering Parkinson's diseaseit's necessary to talk about Gene mutations. Firstly, Mutations are sudden changes in any genetic material of an organism or living being. When mutations are taken into consideration; Specific DNA bases are changed and are affected. Mutations are subjective and can have extensively different consequences based on what gene is affected when and where. This can also be caused by several environmental factors; examples include radiation or extreme weather conditions. Seeing whether Parkinson's disease is heritable; mutations have to studied to be passed on to the next offspring. Sometimes some mutations can only affect the next generation or the next individual that carries them. However, some mutations can affect all the offspringthat are mated by the carrier. Carriers are those individuals that are capable and vulnerable to pass a mutation or a genetic mutation to the next generation. They can carry gene mutations of diseases that may or may not show symptoms. These are usually those who show recessive traits. So what is recessive and what does apply to?

There are alleles in all our bodies that are alternative forms of genes that can either form from mutations or are naturally affected. Alleles can also be called gene variants that pass a trait to the next generation. Alleles are made of two types recessive and dominant. The allele that shows and has an effect on the hybrid or heterozygous organism is said to be Dominant and on the other hand, the allele which has no effect is said to be Recessive. The extensively varied alleles contain varied sequences of bases. This is aroused from mutation.

Mutations can also cause a change in the number of whole chromosomes. The broad gene mutations can affect or change sequences of bases in three different types; which are base substitution, base addition, and base deletion. Base substitution as the name suggests; is when one base is replaced by another base. Base addition is when one base or more bases are added to the sequence. Finally, Base deletion is when one or more bases are deleted from the sequence. Each gene that codes for Parkinson's disease when gets mutated; goes through one of the three processes mentioned of base editing. When Parkinson's disease is considered to be hereditary it is usually from one parent and is known as autosomal dominant. This means that whenever only one part of the gene is altered the parent is a carrier to the next generation causing a vulnerability of Parkinson's disease.

The first gene that is involved and gets depleted in Parkinson's disease is the SNCA gene. The SNCA gene supplies adequate commands in need of the creation of a small protein that is known as alpha-synuclein. At the ends of neurons there are small, tiny gaps called synapse or the synaptic cleft. At the ends or the tips of these neurons are small specific structures called presynaptic terminals. This is where alpha-synuclein protein is found in abundance. In the gaps between the neurons (synapse); the body releases neurotransmitters in small vesicles. The role of alpha-synuclein is that it maintains regulation and a good amount of synaptic vesicles in these gaps. As mentioned earlier that Dopamine depletion plays an important role in Parkinson's disease. What can be the relation between Dopamine and SNCA gene?

The vesicles in the synapse have a specific amount of Dopamine intending to maintain and function the passing of neurotransmitters. The alpha-synuclein protein has a function in the genesis (formation or creation) of the dopamine vesicle. Therefore when there is a mutation in the SNCA gene which is located on the fourth chromosome on the human genome; there is a depletion or shift in levels of alpha-synuclein. Intake affecting dopamine levels and making the human being more vulnerable to Parkinson's disease. This mutation can be base substitution

which is a missense mutation. When more than one allele inhabits a specific gene's, location restricted to a specific population it is known as gene polymorphism. There is a particular single-nucleotide polymorphism in the SNCA gene that can lead to specific and particular mutations which in intake leads to vulnerability of Parkinson's disease. This development of Parkinson's disease can either be autosomal recessive or by the risk of specific dominant mutations.

After looking at mutations and the first gene of Parkinson's disease; the effects of mutations on random genes should also be looked at. Mutations are particularly random and can happen in any given situation given the circumstances. Sometimes one specific mutation can have an enormous effect; However, sometimes many mutations can sum up to a big transformation which each hassmall effects. The more the bases of the gene are affected the more the chance of each being mutated. This intake causes a larger probability of damage to one's genes. This same applies to Parkinson's disease. There is something known as distributions of mutational effects that show how many mutations occur in a given amount of population. Scientists use that to calculate the probability for the same.

The second and one of the most important gene is the PARK2 which helps in the creation and formation of the Parkin protein. This is a particular protein that helps in the recycling of other proteins. As mentioned earlier the autosomal recessive disorder of Parkinson's disease can also be caused by gene mutations. This form of Parkinson's disease which includes autosomal recessive can be caused by what is called as germline mutation on the PARK2 gene. Germline mutation, basically when mutations occur on the germ cells. These are the cells in humans which can be passed onto the next generation. There are two germ cells sperm and ovule. When mutations occur on these they are called germline mutations. For example there is cancer caused by germline mutation which is known as hereditary cancer.

When PARK2 gene gets mutated it can cause a rapid decrease in the dopaminergic neurons in a certain part of the brain called the substantia nigra. Dopaminergic neurons are those same neurons or neurotransmitters that contain or make dopamine. Substantia nigra is a part in the midbrain posterior which has two fixed segments. One of which is very important in containing dopaminergic neurons called the pars compacta. Basically, when PARK2 gets mutated it results in loss of Dopamine in this certain part of the brain. As discussed before intake this would result in an early onset of Parkinson's disease. The gene is located on the Chromosome 6q26 which is also responsible for cancer and can make the body vulnerable. When the gene PARK2 gets mutated to cause Parkinson's disease it disturbs of shifts the ubiquitin-proteasome enhancing system of the body, this makes the body vulnerable to accumulate unnecessary proteins and cause disruptions.

Dopamine has been mentioned many times in this research paper and is an important factor in Parkinson's disease. The other name of Dopamine is hydroxytyramine, it is organic compound formed by involvement of a nitrogen group. Dopamine is the forerunner of the hormone norepinephrine. When nerve impulses are inhibited for transmission in certain parts for the brain such as the substantia nigra and basal ganglia; the dopamine now functions as a neurotransmitter. As mentioned before when there is a decrease in dopamine in the substantia nigra which intake leads to cellular death it causes Parkinson's disease. Norepinephrine which is released at the end of sympathetic nerve fibers; it has the function that helps to increase the muscle contraction of the skeletal which is therefore directly linked to Parkinson's disease.

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The next gene that affects Parkinson's disease is the PARK7 gene or DJ-1 gene. DJ-1 protein reacts to oxidative stress conditions in the body when proteins need to be regulated in redox reactions. The body needs molecular chaperones. Briefly, the proteins helps in protecting cells from oxidative stress. What is this oxidative stress? When free radicals which are any molecules of oxygen that have uneven number of electrons which makes easily react with other molecules this causes oxidative stress. Moreover, DJ-1 helps in binding of proteins in 3-dimensional shape and can also help in refolding of damaged proteins. PARK7 gene mutations make the DJ-1 protein very small and ineffective; This can also change how the amino acid functions disrupting the making of the protein.

DJ-1 causes early onset of Parkinson's disease when it has just started at a tender age. The gene if found on chromosome 1p36. DJ-1 is also very important in homeostasis of mitochondrial calcium and regulation as well as protection of the mitochondrial structure. DJ-1 is very small of only about 20 amino acids and therefore when a change is occurred in such a small structure is causes a lot of harm to the body. An amino acid that makes two disulfide bonds when it pairs with itself it cysteine and DJ-1 needs perfect, conserved activity of this amino acid for all its function. Oxidation of this specific cysteine amino acid occurs in oxidation stress conditions. In all DJ-1 also has many cytoprotective functions that can be proven from the same.

Another gene that's directly linked to the control of the mitochondria and therefore has some relation with DJ-1 or PARK2 is PINK1. A kinase is a certain enzyme that specifically transfers phosphate groups to substrates. PINIK1 as all the other Parkinson's genes supplies specific commands to genesis or making of a protein known as PTEN which is a putative kinase 1. PTEN is a protein which is almost found everywhere in the body inside the cells in the mitochondria. Mitochondria is a cell organelle that help providing energy to all the biochemical reactions that are within the cell. During cellular stress for example oxidation stress the PTEN protein is said to help the mitochondria. PTEN is phosphate and tension which can be really vulnerable in cancer is known to be mutated during the same. Among Parkinson's disease PTEN decrease or insufficiency causes severe mitochondrial abnormalities.

There are two specific regions of the PTEN protein: The first region is called the mitochondrial targeting motif. The second region is known as kinase domain. The mitochondrial targeting motif helps in being the target address for the PTEN protein; it helps it reach the mitochondria and ensures the delivery of the protein. The kinase domain aids the functions of the protein for example it helps in its protective functions of the protein. PINK1 gene mutations causes a drastic change in this kinase domain causing the proteins protective functions. Moreover, if mutations are caused on the mitochondrial targeting motif same would happen to the delivery of the protein to the mitochondria. Therefore when cells are stressed the mitochondria cant do anything except because of the mutations on PINK1 gene. This causes many cells in the brain and the muscles to be affected and in the end many nerve cells are also affected causing Parkinson's disease.

The next gene is the LRRK2; leucine-rich repeat kinase 2. LRRK2 is also a protein like many of the genes that affect Parkinson's disease are proteins. There was Alpha-synuclein mentioned before in this research paper and that is again linked to the LRRK2. This gene also give commands on the genesis or making of the protein dardarin. Some parts of the dardarin protein is associated with leucine-rich regions which help in interactions of proteins with other proteins for example assembling of amino acids or signal transmission over all the proteins together. Dardarin is known for its kinase activity which specifically helps the phosphate group to transfer

ISSN 2350-109X
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to amino acids from the ATP generating energy molecule. LRRK2 is certainly associated with the late-onset of Parkinson's disease and its mutations are studied extensively.

Mutations that occur in the LARRK2 affect the specific amino acids that are replaced by these mutations and therefore affect the analogy and structure of the protein dardarin. Certain mutations that replace amino acids can cause severe damages. For example there is a mutation which replaces the amino acid arginine with amino acid glycine which is a very common form of Parkinson's disease that is specifically originated from the Basque region that is located between Spain and France. Around 7% of the world population show that LRRK2 gene casues familial Parkinson's disease and is directly affected to it. There is also proof of sporadic Parkinson's disease by mutations of the LARRK2. In the protein coding of the exons of the gene LARRk2 at least 128 mutations have found to be occurred which majority of all are said to be base substitutions.

DISCUSSION

The main genes that affect Parkinson's disease have been discussed. Investigations and analytical data of the same has to be discussed and the theory relating to that will also be discussed further in the research paper. The age places an important factor in a person being diagnosed with Parkinson's disease. The risk of getting the disease increase with age. Considering any disease crude prevalence rate (CPR) is taken into account which is basically the new cases per 100,000 of population which gives an approximate number for the new cases. For example if we take 100,000 people. Only 41 of them will get diagnosed with Parkinson's disease in their fourth decade of their life which is in their 40s. However, there will be more than 1900 people out of those 100,000 getting diagnosed with Parkinson's disease. Only about 4 percent of people get diagnosed before the age of 50 which shows its relevance with age and how age plays an important factor in it. Moreover, as the statistics show men are 1.5 times more likely to get diagnosed with Parkinson's disease then women. Statistics show that about 7-10 million people worldwide are currently diagnosed with Parkinson's disease.

America has seen many Parkinson's disease cases overtime and still many are diagnosed with the same. Each year there are approximately 60000 cases of Parkinson's disease that are diagnosed in America. Currently about a million people in the US are said to be living with Parkinson's disease, this is said to rise to about 1.2 million by 2030. America has taken up a project called the Parkinson's prevalence project which ensures resources for each and every citizen having Parkinson's disease. A countries government needs to have data and accurate statistics to know where each Parkinson's disease patient lives, how many people have the disease and what are the required resources needed for the same. This ensures equality between all Parkinson's disease patients. There are two important words that need to be addressed when talking about the same. These are incidence and prevalence. Incidence is basically how many new cases are diagnosed in a given amount of time; this is almost always taken over a year. However, prevalence is not only knowing how many individuals have the disease but also obtaining a measurement of all the individuals.

In our country India; which has the second highest population in the whole world showed a low crude prevalence rate of about only 53 out of 100000 population getting diagnosed with Parkinson's disease. However, in the city of Bangalore; it was seen that the rate was three times in rural areas as compared to urban areas. The CPR of only the city was 41 in rural areas but it

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was only 14 in the urban areas. If we look at the statistics of a specific community in India. The Parsis; we see that it has an CPR of 328 which is higher than most developing countries and developed countries. Age specific CPR for Parkinson's disease go upto 247 above the age of 60 for the generic population. Most sex related CPR studies showed men were more prone to get diagnosed with Parkinson's disease than women. This had an exception of eastern India which showed women were more commonly affected then men in that region. In India mostly the prevalence rate of Parkinson's disease is very low.

If United Kingdom is taken into consideration, every hour one patient is diagnosed with Parkinson's disease. By 2025 the expected prevalence is said to rise by 18% and by 2065 they are said to be almost doubled. The prevalence for idiopathic Parkinson's disease is approximately 128 in the London only; making it one of the highest in the world. Seeing about 10-20% community patients go undiagnosed the idiopathic Parkinson's disease is 200 for every 100000. As discussed before in the document as the age increase the risk of Parkinson's disease increases even more. Therefore in the UK people above the age of 70 have the prevalence of 1500-2000 in every 100000 which is massive. The crude prevalence is about 193 in total of only the city London. If we take the whole UK its about 500 people; there are about 127000 people with the disease currently living over there.

Dr. Rajendra Jhanwar. With MBBS, MD-General Medicine, DM-Neurology. Having experience of 16 years; he is one of Mumbai's top-rated neurologist. He sees patients with severe headache, migraines, epilepsy vertigo, Parkinson's disease, dementia, memory loss etc. Established in the year 2014, he performs nerve conduction study, electromyography tests and special tests regarding Parkinson's disease. I took an interview of him to know more about Parkinson's disease and his say on it.

There were a total of 15 questions asked and the interview went as follows:

I am writing a research paper on investigation in the link between genetics and Parkinson's disease. This is a project for MISA competition. The domain that covers this is Bioinformatics and scientific computing therefore statistics is something that we are looking at. These are the survey questions for Dr. Rajendra Jhanwar, questioned orally by Mohammad Petiwala. Writer of this research paper and orally answered by the doctor:

1. Since how long have you been practicing as a Neurosurgeon?
   I have been in this field for quite sometime meeting different patients almost half of my life. I have a total experience of 16 years with 15 years as a specialist where I could treat them on my own.
2. In these many years approximately how many Parkinson's disease patients have you met and treated?
   It's hard to say there were so many patients I have met that I myself have left track of the same. I have treated Parkinson's disease for a long time seeing people from all age groups having the disease. I would say about 5000 plus or minus 500 patients are approximately the number of Parkinson's patients I have met and treated.
3. Do you think it's a common neurodegenerative disease among Indians?
   Yes absolutely, If I have only seen 5000 patients then its one of the most common neurodegenerative disease in India. Just think how many neurologists are in India and if each

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might have approximately seen 5000 patients then this disease is very common. However, I might say the therapy is difficult and patients need a lot of attention.

4. Which age group have the majority of people affected by this disease?
   By the fourth decade of ones life; A person starts being more prone to the disease and as the age increases the crude prevalence rate and number of people having the disease also increases. If you tell me to give a range then it would be 55-70 years. That will be the range that I have seen maximum patients from.
5. Therefore which age group gets treated to the highest extent?
   I would say this question is too subjective to the patient and truly what's the will power of the patient. However, yes I would say that if its diagnosed at a later stage in the life then it's tougher to treat it fully. Therefore I would say if a patient is diagnosed in his/her 50s then the treating extent is the highest.
6. What are the different stages of this disease?
   I would simply say Mild moderate and very advanced.
7. Is treatment possible for all these stages?
   Absolutely, if the patient has the will power then yes treatment is possible.
8. What are the most common treatments, and which ones do you prefer?
   Dopamine agonists is one of the most common treatments as its drug based and easier to perform on the patient. Many doctors prefer it as they don't have to put a lot of effort and have to wait for the drug to do its work.However, I prefer the Syndopa Plus tablet treatment which comprises of Levodopa and Carbidopa.
9. What has been your experience with the trauma of this disease?
   Very severe as it affects the patient physically, emotionally and financially.
10. Are there any demographics specifically more vulnerable to this disease?
    Debatable question but according to me no there are no demographics more vulnerable.
11. Is physical therapy just as important as medicinal drug treatment?
    Absolutely!
12. Would you say the disease is still to be well understood?
    True, we still don't know exact cause of this disease. All research doctors have tried their best to give an explanation but none have been successful with the same.
13. What are the genes that are mutated and can cause Parkinson's disease?
    PARK gene and LRRK gene. PARK gene mostly causes the dopamine problem; I wont go deep in it as there is a lot to understand. However, I would say the dopamine inefficiency which specifically causes the movement disorders as it affects the specific nerve impulses in the brain.
14. Research has been going on for a long time about the genes that are affected and mutated. According to you, Is Parkinson's hereditary or not? Why do you say so? And can you take examples of the genes that are affected?
    I have would again say this is very debatable and research is still yet to prove everything of genes and hereditary. It takes immense pleasure to answer such interview of students who themselves are researching on the same but I would say only 10% of the patients have hereditary Parkinson's. The gene which I have seen to be always affected is the PARK gene which causes the immense hassle. Research is yet to prove everything. I am just a specialized

doctor helping patients overcome the disease and myself would like to know more if genes are taken in consideration.

15. How does mutation in these genes affect dopamine production because till date its not fully understood why and how does this happen?
    Again same answer for this its yet to prove everything and research is what will provide you with the answer. I would say this is not fully understood and will take many years of ahead research to prove this.

CONCLUSION

In a nutshell, there are many genes that are directly linked with Parkinson's disease in specific chromosomal positions. Parkinson's genetics has come a long way; from where no every scientist doubted its relation to Parkinson's to get a knowledge and understand its specific impact Therefore the discovery of certain genes such as the Alpha-Synuclein or the PARK2 has distinctly shown phenotypes that would affect Parkinson's disease. Parkinson's is more to be a motor disease than a non-motor disease. Research for proving it to be a non-motor disease still continues as there is a definitive diagnostic test involved in doing so. There are a lot of research papers trying to prove the existence of genes in the disease to completely stop it before it affects the body other than just trying to arrest the disease by slowing its effect on each ones body. Doctors for better control of the disease are now switching to methods that help inhaling dopamine directly from the use of medicinal drugs rather than using physical treatment which can affect in the patient in many ways. These are the new delivery methods to restrict the symptoms of the disease rather easily than physical. There have been a study for the gene therapy which is yet to be used by doctors but it does show promising results for Doctors to go ahead with. Moreover, patients with gene mutations will have a easier treatment than those without as Gene mutations are currently only seen in specific genes such as PINK1, PARK2, PARK7 and some more.

REFERENCES

1. No name. "Parkinson's Disease". National Library of Medicine.https://www.nia.nih.gov/health/parkinsons-disease#:~:text=Parkinson's%20disease%20is%20a%20brain,have%20difficulty%20walking%20and%20talking(accessed May. 4, 2021).
2. Dr. Lawrence Loewe. "Genetic Mutation". Scitable by nature education. https://www.nature.com/scitable/topicpage/genetic-mutation-1127/(accessed May. 5, 2021).
3. Donna Krasnewich. "Carrier". National Human Genome Research institute. https://www.genome.gov/genetics-glossary/Carrier (accessed May. 6, 2021).
4. No name. "Types of mutation". Understanding evolution. https://evolution.berkeley.edu/evolibrary/article/0_0_0/mutations_03 (accessed May. 8, 2021).
5. No name. "SNCA gene". National Library of Medicine. https://medlineplus.gov/genetics/gene/snca/ (accessed May. 8, 2021).
6. NevraAlkaniand Arzu Ay. "The Relationship between Alpha-Synuclein (SNCA) Gene Polymorphisms and Development of Parkinson's Disease." Intech Open.

https://www.intechopen.com/books/synucleins-biochemistry-and-role-in-diseases/the-relationship-between-alpha-synuclein-snca-gene-polymorphisms-and-development-risk-of-parkinson-s (accessed May 9, 2021)

7. No name. "The Genetic link to Parkinson's disease". John Hopkins Medicine. https://www.hopkinsmedicine.org/health/conditions-and-diseases/parkinsons-disease/the-genetic-link-to-parkinsons-disease#:~:text=About%2015%20percent%20of%20people,SNCA%20gene%20(see%20below) (accessed May. 10, 2021).
8. SelvarajuVeeriah. "Somatic mutations of the Parkinson's disease associated gene PARK2 in glioblastoma and other human malignancies." Nature genetics. https://www.nature.com/articles/ng.491 (accessed May. 10, 2021).
9. Jamie N. Guzman, Javier Sanchez-Padilla, C. Savio Chan and D. James Surmeier. "Robust Pacemaking in Substantia Nigra Dopaminergic Neuron". US National Library of Medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2784968/#:~:text=Dopaminergic%20neurons%20of%20the%20substantia,structures%2C%20such%20as%20the%20striatum (accessed May. 10, 2021).
10. No name. "Dopamine". Britannica. https://www.britannica.com/science/dopamine (accessed May. 10, 2021).
11. No name. "PARK7 gene". National Library of medicine. https://medlineplus.gov/genetics/gene/park7/ (accessed May. 11 2021).
12. No name. "PINK1n gene". National Library of medicine. https://medlineplus.gov/genetics/gene/pink1/ (accessed May. 15 2021).
13. JieQiong Li, Lan tan and Jin-tin Yu. "The role of LRRK2 gene in Parkinsoism." Biomedcentral. https://molecularneurodegeneration.biomedcentral.com/articles/10.1186/1750-1326-9-47 (accessed May. 20 2021).
14. Chou Chai and Kah-Leong Lim. "Genetic insight into sporadic Parkinson's disease Pathogenesis". US National Library of medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3924245/ (accessed May. 22 2021).
15. No name. "Parkinson's Disease Statistics". Parkinson's news today. https://parkinsonsnewstoday.com/parkinsons-disease-statistics/?cn-reloaded=1 (accessed May. 24 2021).
16. No name. "Statistics". Parkinson's foundation. https://www.parkinson.org/Understanding-Parkinsons/Statistics (accessed May 25 2021).
17. M Gourie-Devi. "Epidemiology of neurological disorders in India: Review of background, prevalence and incidence of epilepsy, stroke, Parkinson's disease tremors.". Neurology India. https://www.neurologyindia.com/article.asp?issn=0028-3886;year=2014;volume=62;issue=6;spage=588;epage=598;aulast=Gourie-Devi (accessed May. 30 2021).
18. A Schrag, Y Ben-Schlomo, N P Quinn. "Cross sectional prevalence survey of idiopathis Parkinson's disease and parkinsonism in London.". International Quality and Safety in HEALTHCARE Europe. https://www.bmj.com/content/321/7252/21.short (accessed June. 1 2021).

19. Lynn M.Bekris, Ignacio F. Mata, Cyrus. P Zabetian. "The Genetics of Parkinsons disease.". US National Library of Medicine National Institutes of Health. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3044594/ (accessed June 8, 2021).
20. No name. "Parkinson's disease: moving forward". A Train Education. https://www.atrainceu.com/content/14-conclusion-and-epilogue (accessed July 1, 2021).