Impact of Lifestyle on the Disease Progression of Parkinson's

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons.)

School of Pharmacy

Brac University

March, 2022

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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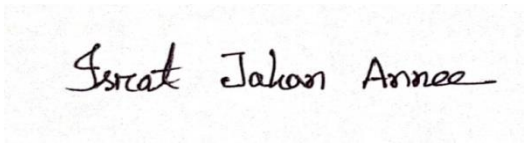

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Approval

The project titled “Impact of Lifestyle on the Disease Progression of Parkinson’s” submitted by Israt Jahan Annee (17346022) of Summer, 2017 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on [30-06-2022].

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Ethics Statement

The study does not involve any kind of animal and human trial.

Abstract

Parkinson's disease is a neurodegenerative illness that causes the nerves in the brain to deteriorate. Shivering, muscular stiffness, sadness, cognitive issues, and sleep problems are some of the symptoms. A molecule called dopamine is considered to be associated to Parkinson's disease. This condition may be caused by a lack of dopamine in the brain. This illness does not have a comprehensive cure. Disease progression may be slowed by maintaining normal dopamine levels. A balanced and nutritious diet, as well as frequent physical activity, is essential. Maintaining a healthy lifestyle, as well as being stress-free, may assist to slow the course of Parkinson's disease. The goal of this review is to show how a healthy lifestyle may assist to slow the course of Parkinson's disease and to identify the most effective and feasible healthy lifestyles for slowing down the disease's progression. Also, bring up the possibility of Parkinson's disease therapy.

Keywords: Parkinson’s disease; dopamine; healthy lifestyle; progression.

Acknowledgement

First and foremost, I would like to express my deepest gratitude towards Almighty Allah for giving me the blessing, the strength, the patience and chance to complete my project work properly.

I am really fortunate that I had the kind and supportive supervision of Dr. Md. Aminul Haque (Assistant Professor of School of Pharmacy of Brac University). His constant encouragement and careful monitoring motivated me to do my work properly. He was very helpful to me whenever I faced any problem in my work and helped me to resolve any kind of inaccuracy in my work. Moreover, I would like to express my special thanks to Dr. Eva Rahman Kabir, Professor and Dean of the School of Pharmacy of Brac University who gave me the opportunity to conduct my project work.

In the end, I acknowledge my sincere gratitude to my parents, friends and seniors for their devotion, support and faith in my ability throughout the whole journey.

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List of Acronyms

PDI	Parkinson's Disease
SNpc	Substantia Nigra pars compacta
L-DOPA	Levodopa
AADC	L-amino Acid Decarboxylase
MAO-B	Monoamine Oxidase B
COMT	Catechol-O-methyltransferase
MT	Methoxy-tyramine
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
PUFA	Polyunsaturated fatty acid
GABA	Gamma Aminobutyric Acid

Glossary

Lewy bodies:	Lewy bodies are protein aggregates that may develop in the brain. When they accumulate, they may interfere with the way brain functions, including memory, mobility, cognitive abilities, emotion, and behavior. Lewy bodies have been detected in the brain tissue of Parkinson's disease patients (PD).
Dopamine:	Dopamine is a naturally occurring substance in the human body. It's a neurotransmitter, which means it transmits information from the body to the brain.
NMDA:	The NMDA Receptor is a glutamate and ion channel protein receptor that is activated when glycine and glutamate bind to it.
SNCA gene:	The SNCA gene encodes alpha-synuclein, a small protein.
A8:	Smallest dopaminergic cells group in rodents and primates, located in midbrain.
A9:	Densely packed dopaminergic cells, located in the ventrolateral midbrain and rodents.
A10:	Largest group of dopaminergic cells located in ventral midbrain tagmentum of rodents.
Cognitive Impairment:	When a person has trouble remembering, learning new things, concentrating or making decision that affect their everyday life is called cognitive impairment.

Chapter 1

1.1 Introduction

Parkinson's disease is a neurological illness in which the small areas of the brain that control movement, posture, and balance are affected. It's a difficult disease with a wide range of symptoms, so not everyone who has it has the same set of symptoms (Kalia & Lang, 2015). Until 70–80 percent of the dopaminergic neurons in the brain have died; there are usually no symptoms or indicators of Parkinson's disease (Weintraub et al., 2015). So understanding out time they think their dopaminergic cells are dying and when they start to show signs of Parkinson's disease could be crucial for the creation of effective neurocytostatic treatment techniques (Emamzadeh & Surguchov, 2018). PD is becoming more well recognized as an illness that impacts more than only movement (Roehr & Bob, 2013). In persons with Parkinson's disease, non-motor symptoms are frequent, and they can influence their cognitive process, social behaviour, relaxation, immune modulation, and tactile are all factors to consider (Robbins TW et al.,2009). As Parkinson's condition worsens, non-motor symptoms become more prominent, as per patients who have been examined for a long time (American Parkinson Disease Association, n.d.). The diagnosis of Parkinson's disease is a life-altering event. Long-term treatment is required to minimize someone's symptoms, and he or she may have to adapt how he or she does everyday duties (Weintraub et al., 2006). Getting treatment for Parkinson's disease may not be able to keep up with how quickly the disease is progressing. Some of them may start to have bad side effects (Robbins TW et al., 2009). They, however, are still good for the patient. At a point where drugs are no longer working, which isn't very often, people stop taking them (American Parkinson Disease Association, n.d.). However, maintaining some daily activities and a healthy routine can reduce the disease progression of Parkinson’s disease.

1.2 Aim of the Review

The goal of this study is to assemble all of the probable Parkinson's disease healthy lifestyles that are predicted to help slow down the illness's development.

1.3 Objectives

The following are the review's goals:

- Accumulate knowledge about Parkinson's disease-friendly lifestyles.
- Gathering data on Parkinson's disease (PD) therapy.
- Determining whether there is a relationship between sedentary behaviour and Parkinson's disease.
- Figure out the most effective and feasible lifestyle for slowing the course of Parkinson's disease**.**

Chapter 2

2.1 Parkinson's Disease

The second most frequent kind of persistent neurological disorder is Parkinson's disease. A gradual degradation of dopaminergic neurons in the SN pars compacta defines it (Emamzadeh & Surguchov, 2018). Parkinson's disease is a motion disorder characterized by the destabilization of the neurological system (American Parkinson Disease Association, n.d.). Neurotransmitters other than dopamine produce PD that affects the parts of nervous system other than the basal ganglia (Wright Willis et al., 2010). Initially, environmental factors were assumed to be the major cause of Parkinson's disease, but new study reveals that the condition is caused by a complex mix of genetics and environment (He et al., 2018). Despite the fact that the very first clear review of Parkinson's disease was reported about two decades ago, the illness's comprehension continues to evolve (Wright Willis et al., 2010). Deficiencies in dopaminergic neurons in the substantia nigra pars compacta might be a precursor to Parkinson's disease(SNPC) (Gába et al., 2016). A shortage of dopamine in the brain's primary motivation center causes a movement disease characterized by classic neurodegeneration motor symptoms (Kalia & Lang, 2015). A broad variety of non-motor symptoms are also linked to Parkinson's disease, some of which occur over a decade prior neurological deficits (Voon & Fox, 2007). Symptomatic therapy using drugs that raise dopamine levels or directly activate dopamine receptors is an important aspect of the therapy for Parkinson's disease (Kalia & Lang, 2015).

2.2 History of Parkinson’s Disease

Although Parkinson's disease was initially identified in 1817, the ailment is today recognized as a medical condition of its own. Parkinson named it "The Shaking Palsy" or "paralysis agitans” (Voon et al., 2010). In his day, tremors were referred to as "agitans." Due to the fact that "palsy" meant "stiffness" and "paralysis" meant "nerve damage," the illness was

recognized as a weakness and tremor problem (Langet al., 2011). Parkinson was considered for his political involvement, geological research, and creation of the truss, which was used preparatory to hernia surgery (Kalia & Lang, 2015). A new research demonstrates that heredity and the environment interact in a complicated way to generate Parkinson's disease, which was previously thought to be largely caused by environmental factors. (Horak et al., 2009) . Although the first precise description of Parkinson's disease was written about two centuries ago, the illness's conceptualization is ever evolving (Berman & Bayati, 2018). In Parkinson's disease, dopaminergic neurons in the substantia nigra pars compacta (SNPC) begin to decline at an early stage(SNPC) (Beraidelli et al., 1986). As a result of the dopaminergic deficiency in the central nervous system, a person will have typical movement disorders. Non-motor symptoms of Parkinson's disease have been related to it as well, and some of these appear almost a decade prior onset of motor symptoms (Ashburn et al., 2007). Symptomatic therapy with medications that enhance dopamine concentrations or directly activate dopamine receptors is the fundamental to the treatment of Parkinson's disease (Kalia & Lang, 2015).

2.3 Pathogenesis of Parkinson’s Disease

Even though the severity of the deficiency does not affect Parkinson's disease tremor once it is established, the nigrostriatal insufficiency is necessary for the tremor to occur in humans (Poletti et al., 2012). In contrast to stiffness and akinesia, the clinical severity of Parkinson’s disease tremor is unrelated to clinical disease progression (Verbaan et al., 2009) (Bergman & Deuschl, 2002). For example, there is a conflict about whether peripheral nervous system origins or limbic system origins, whether intrinsic cellular oscillators or network oscillators govern brain function, and if sickness in the basal ganglia is linked to cerebellar–thalamic activity (Marsh et al., 2004). Recent study reveals that abnormal synchronous oscillating activation of neurons in the basal ganglia is the most probable source of parkinsonian

symptoms (Riedel et al., 2010). In Parkinson's disease, peripheral variables have a moderate role in the development, maintenance, and regulation of tremor and other symptoms (Dawson TM et al.,2004). These oscillations are probably caused by basal ganglia-thalamo-cortical loops (Berman & Bayati, 2018). Other neural structures and systems, however, regulate the basal ganglia loops, and changing these loops via cerebellothalamic connections and other modulator neurotransmitter systems entrains the incorrectly synced oscillations (Mandal et al., 2019). While the basal ganglia loops themselves are controlled by other brain structures, such as the cerebellothalamic connections and other modulator neurotransmitter systems, the poorly synchronized oscillations may be retrained by modifying these other neural structures and systems (Bergman & Deuschl, 2002) .

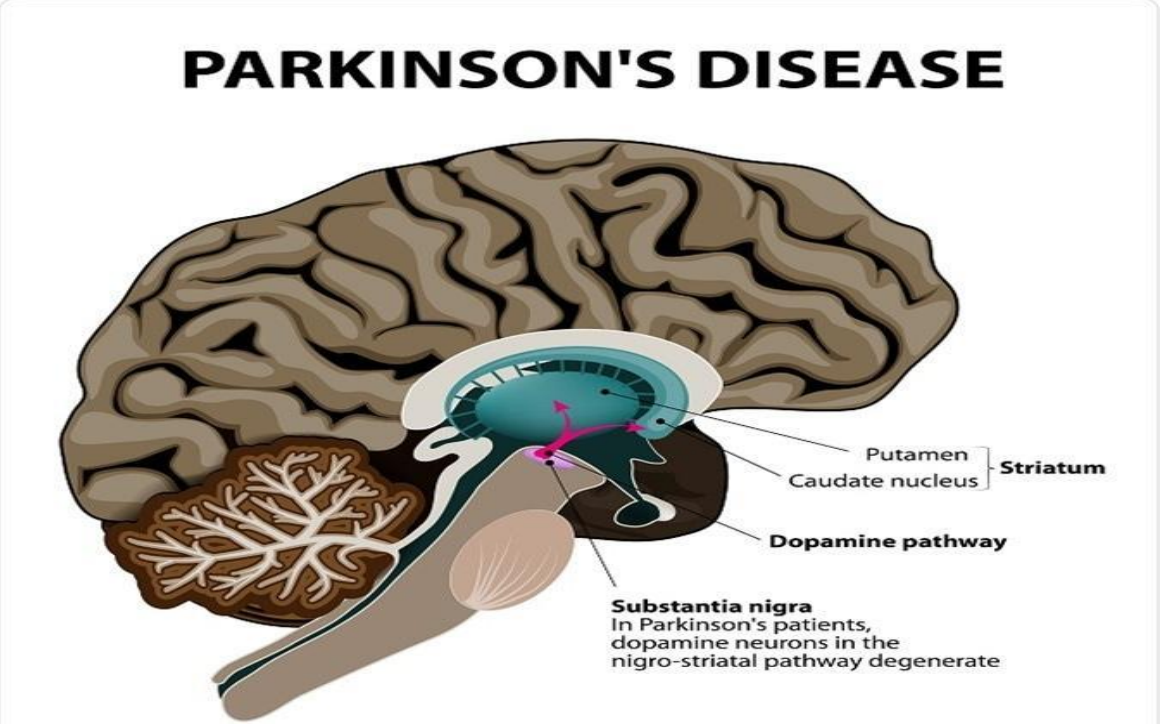

Figure 1*: In Parkinson's disease, brain cells in the substantia area drastically decrease, yielding to the illness's symptoms.There is a region in the brain that controls the production of dopamine. Dopamine is a chemical messenger that helps the brain coordinate activity between two locations. For illustrate, it controls muscular activation by linking the midbrain with the thalamus. A lack of steroid hormone in the dopaminergic neurons causes the nerve cells to "fire" uncontrollably. This makes the individual*

incapable of controlling or directing their own motions. As nothing more than a consequence above, PD is synthesized. Gradually, more brain and nervous system regions deteriorate, limiting movement (Mandal 2019).

2.4 Symptoms of Parkinson's Disease

Parkinson's disease symptoms and indications usually develop when 70–80% dopaminergic neurons have been affected (Brown et al., 2006). To develop appropriate immunomodulatory treatments, detecting individuals between the predicted onset of neurotransmission cell loss and the presence of chronic parkinsonism may be crucial (Emamzadeh & Surguchov, 2018). In Parkinson's disease, symptoms start to show up 7 over time, muscle spasms occur frequently in just one hand, however the disease also causes soreness or slowness of movement (Armstrong & Okun, 2020). Another thing that can happen is that the clinical features of PD can be different for each person (Berman & Bayati, 2018). Early signs may be small and go unnoticed, so it's important to pay attention (Marsh et al., 2004). As the symptoms spread to both sides, they tend to be worse on one side of your body than the other (Solla et al., 2012). This is true even if the symptoms spread to both sides (Marsh et al., 2004). Parkinson's patients may have subdued mobility (bradykinesia), tight muscles, poor body posture, tremor, and abnormalities in writing and speech (Leeman & Potenza, 2011). During Parkinson's disease, some brain nerve cells (neurons) degenerate or die (Kalia & Lang, 2015). Several of the indications originate from dopamine-producing neurons malfunctioning in the brain (Solla et al., 2012). Insufficient dopamine causes abnormal brain activity, leading to decreased movement and other Parkinson's symptoms (Leeman & Potenza, 2011)

2.5 Etiology of Parkinson’s Disease

According to a recent study, Parkinson's disease is caused by a complicated mix of heredity and environment (He et al., 2018). Parkinson's disease is now considered slow moving neurological diseases that affects numerous brain areas and appears in diverse ways (Kalia & Lang, 2015). Another factor contributing to Parkinson's disease is the loss of dopamine-producing neurons and a consequent shortage of dopamine in the brain's locus coeruleus (LC) (Rana et al., 2013). Poor movement and other Parkinson's symptoms are caused by dopamine insufficiency (He et al., 2018). The origin of Parkinson's disease is unknown, while genes, environmental triggers, Lewy bodies, and Alpha-synuclein inside Lewy bodies all seem to play a part (He et al., 2018). A genetic abnormality may be the root cause of Parkinson's disease, as per new study (Rana et al., 2013). Although they do occur from time to time, they are not common until a large number in a family is affected by Parkinson's disease (Kalia & Lang, 2015). In addition, although the risk is modest, long-term exposure to certain compounds or environmental elements may increase one's chance of getting Parkinson's disease (Sun et al., 2012). Microscopic Parkinson's disease indicators have also been shown to be aggregation of particular substances in brain cells (Martínez et al., 2015). Researchers believe that the origin of Parkinson's disease may be explained by studying Lewy bodies (Sun et al., 2012). Alpha-synuclein, a naturally occurring and widely dispersed protein, has been found in Lewy bodies, but experts believe it is vital (a-synuclein). All Lewy bodies contain it in a clumped form, which cells are unable to break down (Kalia & Lang, 2015).

2.6 Stages of Parkinson’s Disease

There are five stages of Parkinson’s disease (Uttekar, 2021). They are;

- Stage-I: At this phase, minor symptoms that do not disrupt regular activities. Symptoms of movement on only one side of the body (for example, tremors, rigidity, and

bradykinesia) (unilateral), issues with posture and balance that are not serious, walking is a little difficult, slightly altered facial expressions (Uttekar, 2021)

- Stage-II: Symptoms worsen at this point, making daily activities more difficult (Fritsch et al., 2012). The individual, on the other hand, is capable of self-care. Movement signs and symptoms walking difficulties, inability to balance, poor posture Faces that have less expressions (Uttekar, 2021).
- Stage-III: Stage III symptoms are more severe than Stage II symptoms, which are significantly less severe. The individual, though, is still on their own (Uttekar, 2021). This stage is marked by loss of balance and movement (Fritsch et al., 2012). Eating, bathing, and dressing are all highly restricted (Uttekar, 2021)
- Stage-IV: Living on one's own is nearly impossible at this point because he/she can't eat, bathe, dress, sleep, or wake up (Uttekar et al., 2021). Some people can stand but need help moving (Fritsch et al., 2012). A walker can assist you in moving about without falling (Uttekar, 2021)
- Stage-V: This severe stage may cause people to be unable to stand on their own. The person is unable to get out of bed and must rely on a wheelchair to get around (Uttekar, 2021). Some of the symptoms at this stage include delusions (beliefs that don't alter no matter how much evidence contradicts them) and hallucinations (seeing, feeling, or hearing things that aren't there) (Fritsch et al., 2012). People who are unable to think or recall information Weight loss, as well as a slew of sleep issues It's difficult to see (Uttekar, 2021).

2.7 Risk Factors of Parkinson's Disease

Parkinson's disease may be carried on by a variety of circumstances. Only a tiny proportion of young people are diagnosed with Parkinson's disease (Ibba FC et al.,2012). Beginning in midway or late life, the risk increases with age (Sun et al., 2012). In most cases, adults over the

age of 60 are struck down by the condition (Butt et al., 2018). Having a close family member with Parkinson's disease significantly increases the risk of having the condition. Unless one has a large number of patients with Alzheimer’s disease relatives in their family, the odds of developing the condition are quite minimum (MacPhee & Stewart, 2012). Men are more prone than women to develop Parkinson's disease (Brown et al., 2006). Parkinson's disease may also be exacerbated by long-term exposure to weed killers and pesticides (Uttekar, 2021).

Chapter 3

Current treatment of PD

It has been particularly challenging to evaluate clinical progress toward Parkinson's disease modification because of the illness's slow progression (Uttekar, 2021). Clinical endpoints including such attitude, identity of activities of daily life, and motor evaluation have been included into the Unified Parkinson's Disease Rating Scale (UPDRS) thus far (Palamara et al., 2017). Imaging data (e.g. DAT, SPECT) have been linked to UPDRS modifications, which may provide quantified, objective assessments of effect on pharmacological and biochemical outcomes involved with Parkinson's disease development in the future (Fan et al., 2020).

3.1 Oral Parkinson’s Disease Therapies

All currently approved therapies for Parkinson's disease aim to enhance striatal dopamine levels in order to ameliorate the concomitant motor deficits. Unfortunately, none of these approaches are long-term remedies since their efficacy reduces as dopaminergic neurodegeneration progresses. Drugs like the ones listed below are now being utilized to treat Parkinson's disease symptoms by controlling dopamine levels (Fahn, 2005).

3.2 Dopamine Precursors

Aromatic L-amino acid decarboxylase (AADC) biosynthetically converts levodopa (L-DOPA, 2) to dopamine, which is then given to Parkinson's disease (PD) patients as a dopamine booster. More than 80% of levodopa users who have been on the drug for more than ten years have dyskinesia and "off" periods (Palamara et al., 2017). Carbidopa is typically used in concert with L-DOPA to limit systemic metabolism and maximize central exposure, allowing lower dosages of L-DOPA to be administered while lowering unpleasant effects like nausea (Uttekar, 2021).

3.3 Dopamine Agonists

By acting on dopamine receptors, dopamine agonists enhance the effects of dopamine. Apomorphine, bromocriptine, ropinirole examples of recognized medications that activate the dopamine receptors and are suggested for treating Parkinson's disease. Each of these drugs is most efficient as a D2-like receptor agonist, with some demonstrating 5-HT, -adrenergic, and adrenergic antagonistic activities (Uttekar, 2021).

3.4 Monoamine Oxidase B (MAO-B) Inhibitors

Due to dopamine levels in the brain are elevated by MAO-B inhibitors, motor symptoms are reduced in Parkinson's disease patients, who are prescribed these drugs. Among the MAO-B inhibitors that have received FDA approval are the irreversible inhibitors selegiline (Uttekar, 2021).

3.5 Catechol-O-Methyl Transferase (COMT) Inhibitors

Dopamine is converted to 3-methoxytyramine (3-MT, 10) by the enzyme catechol-O-methyl transferase (COMT), which is then oxidized by the enzyme MAO-B to create homovanillic acid. Dopamine levels in the brain are raised by COMT inhibition, which, like MAO-B inhibition, has been utilized in Parkinson's disease treatment for the last two decades and is an effective combo therapy. Entacapone and tolcapone, two COMT inhibitors that are currently considered standard of care (Fahn, 2005).

3.6 Anticholinergics

Patients with tremors and dystonia may benefit from anticholinergics, which modify the function of acetylcholine, a key neurotransmitter in movement regulation. Cholinergic action is inhibited by benztropine and trihexyphenidyl, two authorized antiparkinsonian drugs (DeKosky & Marek, 2003).

3.7 Miscellaneous Approved Therapies

A variety of complementary and alternative therapies are used in order to alleviate the symptoms of Parkinson's disease. After being utilized as an antiviral, the NMDA glutamate receptor inhibitor amantadine is currently used to treat Parkinson's disease dyskinesia, albeit its efficacy has been called into doubt (DeKosky & Marek, 2003). A new norepinephrine prodrug, droxidopa, has been licensed for the treatment of Parkinson's disease-related neurogenic orthostatic hypotension, MSA, and complete autonomic failure in the United States (Fahn, 2005). The 5-HT inverse agonist, pimavanserin, has been used to treat Parkinson's disease-related hallucinations, delusions, and psychosis. Additional treatments for dementia and Parkinson's disease are also available, including rivastigmine (a kind of acetylcholinesterase inhibitor) (Dorsey & Bloem, 2018).

Chapter 4

Link between Sedentary Lifestyle and Parkinson’s Diseases

People who smoke are less likely to get Parkinson's disease (PD), according to epidemiological research (Checkoway et al., 2002). Parkinson's disease is strongly linked to smoking, with smokers having a lower risk of the illness than nonsmokers, according to a thorough evaluation of the current literature (Marras et al., 2016). Smoke's positive influence on the human body is now being investigation (Zhang et al., 2014).As a result of epidemiological studies showing a lower incidence of Parkinson's disease in those who smoke, nicotine is being explored (Ray Dorsey et al., 2018). We have here one of the most exciting discoveries in Parkinson's disease research, without a doubt (Brown et al., 2006). For two reasons, nicotine is a suitable alternative to cigarette smoke, which contains hundreds of components. In the striatum, where dopamine neurons are most destroyed in Parkinson's disease, nicotine activates them. Second, nicotine exposure shields experimental animals' brains from harm (Checkoway et al., 2002). Over the last half century, more than 40 different studies have shown a connection between tobacco and Parkinson's disease (Voon et al., 2011). Smoking's long-term health consequences are also dose-dependent and depending on the amount of cigarette-pack-years that one has smoked (Racette et al.,2010). Parkinson's disease affects the nigrostriatal dopaminergic neurons (Chinta et al., 2013). The ensuing effects of nicotine would be affected if denervation altered nACh receptors, hence this is a big concern (Checkoway et al., 2002). Numerous other web pages Some nACh receptor-targeting drugs may be more effective than others. Because A6p nACh receptors are the most sensitive to agonist-induced activation, they may be especially important (Quick, 2004). A possible neuroprotective effect of smoking is to diminish the brain's MAO-B enzyme activity, which might be beneficial for those with brain damage (Zhang et al., 2014). It is possible that MAO-B, which catabolizes dopamine, may activate neurotoxicants in the same way as the well-known experimental PD-inducing drug, MPTP. Dopaminergic system

damage from MPTP may be reduced by an MAO B inhibitor found in tobacco, 2,3,6-trimethyl-1,4-naphthoquinone. MPTP and nicotine have been used in similar research with varying degrees of success (MacPhee & Stewart, 2012). In numerous European and American case-control studies, caffeine use was shown to reduce the incidence of Parkinson's disease (Checkoway et al., 2002). The risk of developing Parkinson's disease (PD) was shown to be negatively associated to beer consumption instead of wine or alcohol use, and this connection was found to be more pronounced in men than in women, according to a recent research (Zhang et al., 2014).

Chapter 5

Impact of Inactive Lifestyle on PD

Children are becoming more interested in modern technologies (Radesky et al., 2015). Smart phones and tablets have become an indispensable part of everyday lives due to their recent popularity (Engberg et al., 2019). According to the General Authority of Statistics (GAS), 98.44 percent of Saudi households or families have televisions, computers, internet access, and smart devices (Mesman et al., 2013). All-cause mortality, childhood obesity, Parkinson's disease, Alzheimer's disease, and type 2 diabetes may be traced back to technology usage (Radesky et al., 2015). Metabolic syndrome and a broad range of medical and psychological diseases have also been connected to technology-dependent children. Because technology disrupts children's daily activities, it might lead to a decline in regular exercise (Kenney & Gortmaker, 2017). Physical inactivity has been connected to an estimated 3.2 million deaths globally each year, considering it a prone for high mortality rates (Mesman et al., 2013). As well as promoting healthy blood pressure and blood glucose levels and better sleep and immune system response, regular physical exercise is essential for a healthy body (Oswald et al., 2020). An hour of moderate to intense physical exercise every day, as recommended by the WHO, is an absolute need for a growing child (Mesman et al., 2013). According to the findings of this research, children who spend more than five hours a day on their digital gadgets are more prone to be sad and to develop physical rigidity as well as cognitive (Kenney & Gortmaker, 2017). An hour of moderate to intense physical exercise every day, as recommended by the WHO, is an absolute need for a growing child (Radesky et al., 2015). According to the results of the present research, those who used their electronic devices for 5 hours or less were more active than those who used them for 6 hours or more (Moore et al., 2020). As a result, people may have sleep disorders, sadness, rigidity of the body and muscles, high blood pressure, and poor cognition (Radesky et al., 2015). It is well known that circadian (roughly 24-hour) cycles

regulate activities like hormonal balance, sleep/wake schedules, or mental activity capacity and are managed by the internal clock, which is situated in the caudate nucleus of the brain (Mesman et al., 2013). Advances in contemporary technology, such as televisions and laptops, allow for and even promote later sleep schedules and extended times of midnight arousal, which are organically linked to modern lifestyle factors that affect sleep (Oswald et al., 2020). As a result of being glued to their smartphones, tablets, and laptops for long stretches of time, many individuals are developing muscular stiffness and dementia as a result of their inactivity. They also lack the energy and nourishment to regularly exercise (Kenney & Gortmaker, 2017).

Chapter 6

Healthy Lifestyle for Parkinson’s Disease

6.1 Diet

According to an increasing amount of epidemiological research, nutrition has an effect on the progression of neurodegenerative diseases like Parkinson's disease (both positively and negatively (Uyar & Yildiran, 2019). One of the most major risk factors for neurological illnesses such as Parkinson's disease is a Western diet (Checkoway et al., 2002). Saturated and omega-6 fats, processed carbohydrate, excessive salt, and low intake of omega-3 fats and fiber define the Western diet, which has significant intake of calories of energy-dense foods (Bonifati, 2012). Patients with Parkinson's disease who have a greater calorie consumption of macro and micronutrients are more likely to suffer from PD-related symptoms, according to a new study (Leeman & Potenza, 2011). Diets high in animal saturated fats have been linked to an enhanced danger of Parkinson's disease in several investigations (Brown et al., 2006). Canning fruits and vegetables, consuming caffeinated drinks and fried meals such as steak or ice cream, and eating cheese have all been linked to a faster development of Parkinson's disease (all characteristic of the Western diet) (Checkoway et al., 2002). A "healthy" diet, on the other hand, has really been linked to benefits for those with Parkinson's disease (Chinta et al., 2013). Those who eat a Mediterranean diet have a decreased chance of developing Parkinson's disease (Brown et al., 2006). All of the following are associated with better health: fresh fruits and vegetables; fresh nuts and seeds; non-fried fish; extra virgin olive oil; extra virgin wine and coconut oil; and extra virgin olive oil, alcohol, coconut oil, and fresh herbs and spices (Jackson et al., 2019). Flavonoids, which are found in tea, cherries, apple juice, red wine, and orange/orange juice, have been linked to a reduced incidence of Parkinson's disease (Fritsch et al., 2012). Additionally, polyunsaturated fatty acids (PUFA) are connected to lower risk of

Parkinson's disease (greater ingestion of 3 fatty acids is linked to lower risk of Parkinson's disease). This shows the impact of dietary fat intake on the brain (Uyar & Yildiran, 2019). The gut microbiota may impact Parkinson's disease initiation and growth via a variety of methods, including the primary consumption of dietary components (e.g., vitamins, lipids) (Jackson et al., 2019). The gut microbiota's shape and metabolic activity may be determined solely by nutrition. Parkinson's disease risk may be reduced by drinking coffee and consuming caffeine. Coffee and smoking have been shown to lessen the risk of Certain diseases in a daily dosage manner in early trials (Checkoway et al., 2002). Parkinson's disease is less common in men and women who use coffee, according to recent research (Jackson et al. 2019). Caffeine (from coffee) and nicotine (from smoking) have been proven to ameliorate Parkinson's disease symptoms in MPTP mouse models. Aside from the NLRP3 inflammasome-reducing chlorogenic acid, coffee also includes polyphenols that have been found to be neuroprotective and support healthy microbiota metabolism (Uyar & Yildiran, 2019). In two distinct investigations, the microbiota was implicated in the therapeutic benefits of caffeine in reducing the risk of Alzheimer's disease (Fritsch et al., 2012). Is there a relationship between Parkinson's disease and the usage of alcohol (Wright Willis et al., 2010). Two major prospective studies found no link with frequent alcohol use and Parkinson's disease (Jackson et al., 2019). A protective association between alcohol usage and Parkinson's disease, on the other hand, was discovered in a large-scale study (Checkoway et al., 2002). Another research found a relationship between excessive alcohol use and a lower incidence of Parkinson's disease." According to a recent review of all liquor studies, prospective studies found no link between alcohol usage and Parkinson's disease, with two studies suggesting an elevated risk with frequent alcohol use and the condition (Jackson et al., 2019). There was a greater likelihood of finding a protective effect in case-control studies. Moreover, alcohol has been demonstrated to increase intestinal leakage and harm the microbiota in the colon (Wright Willis et al., 2010).

As a consequence, there seems to be no conclusive evidence that drinking alcohol increases the chance of developing Parkinson's disease (Fahn & Cohen, 1992). Dairy consumption has also been linked to an increased risk of Parkinson's disease. Many studies have connected a high intake of dairy products in total to a higher risk of developing Parkinson's disease (Jackson et al., 2019). Dairy and milk intake has been linked to Parkinson's disease in a research conducted in Greece. Dairy consumption is associated with a greater risk of Parkinson's disease in other recent research (Fahn & Cohen, 1992). A research done in Hawaii found a connection between decreased synaptic integrity in the SN at autopsy and consuming over than two glasses of milk each day (Brown et al., 2006). No evidence exists to support the hypothesis that pesticides in milk are to blame for these correlations (Jackson et al., 2019). Parkinson's disease may be worsened by microbiome bacteriophages, particularly those linked to the Lactococcus bacteria present in dairy products. This theory was supported by a recent research (Fahn & Cohen, 1992). The data isn't strong enough, however, according to a new manuscript on dairy products and Parkinson's disease, to justify widespread warnings about the hazards of dairy products (Jackson et al., 2019). Several circumstances, including poor nutrition, antibiotic usage, aging, and illness, may change the metabolism of microorganisms, leading in the buildup of -syn in the intestinal mucosa cells of the host. According to growing evidence, the quantity, category, as well as balance of nutritional macronutrients (carbs, protein synthesis, and lipids); an increased consumption of veggies, fruit and vegetables, and omega 3 fatty acids and healthy diet patterns such as the Dietary pattern may all have a significant beneficial effect against Parkinson's disease (Uyar & Yildiran, 2019). Recent research has shown that alterations in the intestinal microbiota may have an impact on the visual cortex biophysical, behavioral, and cognitive processes (Jackson et al., 2019). An intricate bidirectional communication system, the GBA, conveys biological, immunosuppressive, and neuronal messages from our stomachs to our brains through the GBA. A few examples of GBA include cytokines, the synthesis of

bacterial metabolites, and signal stimulation of the brain through the vagus nerve. This axis is also responsible for regulating digestion under physiological settings (Checkoway et al., 2002). Many illnesses, including mental health difficulties, have been linked to axis dysregulation, gut dysbiosis, and inflammation (anxiety and depression). According to results from a research conducted on germ-free (GF) mice, the gut microbial community and bacterial metabolites are involved in causing Parkinson's disease via modifying brain function (Jackson et al., 2019). Motility control and anxiety are both affected by the signals activated by microbial colonization. Serotonin, acetylcholine, melatonin, GABA, catecholamine, and histamine are all produced by the gut flora. Controlling blood flow, intestinal motility, absorption of nutrients, the digestive immune system, and the microbiota are all impacted by these neurotransmitters. A variety of gastrointestinal symptoms may be triggered by these neurotransmitters, particularly in diseases like irritable bowel syndrome and Parkinson's disease (Jackson et al., 2019). Even though Parkinson's disease has been connected to dysbiosis, it's unclear whether alterations in the microbiome are to blame for the disease's pathology (Uyar & Yildiran, 2019). Researchers transplanted microbiota from Parkinson's sufferers and healthy controls into categories of GF recipients. There was higher -syn-mediated motor impairment in the microbiomes of Parkinson's disease patients. Parkinson's disease may be associated with alterations in the microbiome and its byproducts through the gut-brain axis, according to research. The vagus nerve may allow -syn opathy to migrate from the ENS to the brain. The vagus nerve carries the accumulated -syn to the CNS. -syn buildup in the brain has been associated to neuronal damage, neuronal injury, and neuronal loss. In Parkinson's disease, gut microbial dysbiosis affects brain function (Checkoway et al., 2002). Patients with Parkinson's disease have altered intestinal microbiota and microbial metabolites. Dietary supplements containing probiotic bacteria may influence gut microbiome composition and epithelial integrity as well as pro-inflammatory responses (Dorsey & Bloem, 2018).

Antibiotics, poor nutrition, pathogens, and other factors may cause intestinal cell plexus pathology, leading in inflammatory processes, oxidative stress, and reduced mucin and SCFA, ultimately ending in -synuclein production (Fritsch et al., 2012). SCFAs (non-digestible carbs) may help treat Parkinson's disease by increasing gastrointestinal motility and decreasing ENS activity, respectively (Verbaan et al., 2009). These fatty acids are necessary for the construction and function of neurological cell membranes as well as synapses (Inzelberg et al., 1998). These fatty acids are necessary for the construction and function of neuronal cellular membrane and synapses (Checkoway et al., 2002). Prebiotics have been shown to help with coronary heart disease, type 2 diabetes, appetite management, obesity, cancer, immune function, and inflammation (Sun et al., 2012). It may help constipated Parkinson's patients since it affects microbiota and encourages bowel motions (Llorca et al., 2016). Given their ability to influence the microbiota composition, prebiotics and probiotics cohabitation may be a therapeutic method for preventing and treating several diseases, including Parkinson's (Uyar & Yildiran, 2019)

6.2 Physical Exercise

Working out may help reduce symptoms of Parkinson's disease. Parkinson's disease may be prevented and treated with regular physical exercise (Fan et al., 2020). People's behaviour and cognitive capacities in daily life are affected by Parkinson's disease, which is seen in the illness's impact on physical activity (Poletti et al., 2012). Physical activity levels of Parkinson's disease patients fluctuate throughout time, although in the initial stages of the illness, they are similar to those of healthy controls (Chastin et al., 2010). Prospective epidemiological studies suggest that physical exercise may help lower the risk of Parkinson's disease in males, although the underlying mechanisms are still unclear (Fan et al., 2020). Men's health researchers from the Harvard Alumni Health Study disprove the hypothesis that exercise might help men prevent

Parkinson's disease (Yang et al., 2016). A research with a lower sample size shows that physical exercise has no effect on Parkinson's disease and may even be harmful (Oswald et al., 2020). According to a research of 143,325 CPS-II-N participants, intense exercise was connected to Parkinson's disease in both men and women, although moderate to vigorous activity reduced the risk of Parkinson's disease by a statistically significant margin (Latt et al., 2009). At ages 35-39 or in the preceding 10 years, higher levels of moderate to vigorous exercise reported in 1996-1997 were likewise related with a decreased rate of Parkinson's disease after 2000, according to the analysis of 213,701 individuals in the NIH-AARP Diet and Health Study cohort (Giovannoni et al., 2000). The nonmotor functions of Parkinson's disease patients may be improved by physical exercise therapy. Exercise has been shown to enhance cardiac sympathetic control in Parkinson's disease patients, although the effects on other systems are still unknown at this point (Fan et al., 2020).Resistance training, qigong, and other forms of physical exercise may help individuals with Parkinson's disease (Fan et al., 2020). For those with Parkinson's disease, the improvement in cognitive function is another advantage of regular physical exercise (Latt et al., 2009). No demented individuals having mild to moderate Parkinson's disease showed any improvement in attention or working memory after 24 months of increased resistance training, according to David et al (Sun et al., 2012). Participants' illness sensitivity, spatial awareness, stability, and executive function all improved after they practiced tango, according to research by McKee and Hackney at the University of Pennsylvania (Chastin et al., 2010). For 12 weeks, Cruise et al. concluded that greater aerobic and anabolic exercise improved executive function in the frontal lobes, which is in line with other studies on this topic. Parkinson's disease sufferers between the ages of 50 and 70 who undergo Feldenkrais-based physical therapy may benefit from 50 sessions, according to researchers (Tomlinson et al., 2012).

6.2.1 Yoga

Yoga may help people improve their walking ability and reduce tremors (Lamont et al., 2012).There are many different styles of yoga, some of which are high-intensity and fast-paced, while others are softer and low-impact (Amano et al., 2013). Yoga may assist to stretch tight muscles, increase flexibility, and improve posture, all of which can help with managing instability issues (Palamara et al., 2017).

6.2.2 Pilates

Despite their similarities, Pilates and yoga are two distinct types of exercise that concentrate on different aspects of physical growth (Sun et al., 2012). Pilates enhances coordination and balance, which are both essential for mobility (Lamont et al., 2012). This is a low-impact exercise that is comparable to yoga (Gába et al., 2016). Both yoga and Pilates may help with anxiety, which is a symptom of Parkinson's disease (Fan et al., 2020).

6.2.3 Walking

Regular aerobic exercise improves several Parkinson's disease symptoms that limit physical skills, such as poor walking, balance and strength difficulties, grip strength, and motor coordination (Lamont et al., 2012). Regular walking training improved normal walking speed and lengthened stride length, which tends to shorten with Parkinson's disease (Lamont et al., 2012). According to researchers, brisk walking sessions increased motor function and mood, attention/response management, fatigue reduction, cardiovascular fitness, and gait speed (Chastin et al., 2010).

6.2.4 Daily Routine Activity

Parkinson's disease may be alleviated by physical activity. Researchers Mehrholz et al. and Herman et al. found that running improved gait, fitness, and safety in a crash test (Fan et al., 2020). A tremor or sluggish stride might cause Parkinson's disease sufferers to become overly concerned about losing their stability and collapsing or spilling items, which can lead to an even more inactive lifestyle (Fahn & Cohen, 1992). Despite the fact that doctors agree that setting out time for physical activity is a vital part of keeping patients healthy and active, new research reveals that exercising regularly may be just as important as going to the gym (Ashburn et al., 2007). Motor symptom degradation may be minimized by engaging in regular tasks such as cleaning dishes, folding clothes, doing garden work, and shopping (Fan et al., 2020).

6.3 Stress Management

6.3.1 Cognitive Enrichment

Even while cognitive symptoms are not experienced by everyone with Parkinson's disease, they are prevalent (Fidani et al.,2016). Only a small number of Parkinson's disease sufferers show signs of cognitive impairment (Schrag et al., 2017). It is possible for certain persons to suffer from cognitive impairments, which may have a negative impact on their everyday lives. Parkinson's disease patients with mild cognitive impairment make from 20% to 50% of the population (American Parkinson Disease Association, n.d.). Dementia in Parkinson's patients is a mystery because of the lack of research on the underlying causes (Fritsch et al., 2012). Changes in neurochemical signals may affect how information is transmitted between various sections of the brain (Oswald et al., 2020). Along with dopamine, neurochemical signals such as acetylcholine, serotonin, and norepinephrine have a significance in cognition, memory,

attention, and mood (Fan et al., 2020). Duringpostmortem investigation, abnormal protein accumulations known as Lewy bodies were detected in neurons in brain regions important for cognitive processing. Co-occurring strokes or "mini-strokes,"along with Alzheimer's pathology, are further possibilities. Managing cognitive impairment in Parkinson's disease depends on the onset and severity of the disorder. Non-pharmacological treatments for cognitive impairment in Parkinson's disease are also available (Latourelle et al., 2009). These methods are intended to aid patients with their day-to-day activities, as well as their mental abilities, relationships, and general well-being (Ray Dorsey et al., 2018). Reminders for patients to take their medications might include clock alarms, timers, and pill reminders (American Parkinson Disease Association, n.d.). In order to keep track of events and time, executive function techniques include methods such as dividing work into digestible parts, creating "to do" lists, daily planners, and alarms (Domen et al., 2019). It's essential to keep to a regimen for everyday work and physical activity. People may mark the drawers so that they know where to find anything from cutlery to glasses to your keys at all times (Marsh et al., 2004) .Patients are more likely to respond positively if they are given options, signs, or yes-no responses, even if they have difficulty finding words or think slowly. Parkinson's disease sufferers must maintain their brains and bodies in shape as they age by engaging in both physical and mental "training.". Research shows that rats placed in "enriched environments" with toys and other stimulating items develop and learn more rapidly than rats kept in "numbing" circumstances, despite the fact that the specific process is still unclear. The thought of "use it or lose it" comes to mind since it is a cognitive concept (Fritsch et al., 2012). Mental interests include puzzles, card or board games, reading a book, attending lectures or concerts, or learning a new skill (Latt et al., 2009). Mental stimulation requires social connection (Horak et al., 2009). It is possible to participate in a number of these activities with the help of loved ones or friends (Hackney & Earhart, 2008).

6.4 Mind body Practices

6.4.1 Meditation

Meditation and yoga also helps Parkinson's patients improve their motor skills, mobility, balance, flexibility, and upper and lower limb strength, as well as reduce their fear of falling (Palamara et al., 2017).

6.4.2 Dancing

According to Aguiar et al., people with Parkinson's disease benefit from regular dancing in terms of balance and movement (Yang et al., 2016). If a person who likes to move his/her body, dancing to a pulsating beat might help him/her improve his/her motor control and blood flow (Marras et al., 2016). As a consequence of greater brain plasticity, physical mobility, balance, and cognition are all enhanced (Pang & Mak, 2009). Patients with moderate to severe Parkinson's disease may benefit from Tai Chi and Qigong practice (Hackney & Earhart, 2008).

6.4.3 Games

People with Parkinson's disease may benefit from computer-based physical therapy games, according to a study sponsored by the UCSF School of Nursing and Red Hill Studios, a California game producer. UCSF and Red Hill were the first US research teams to get government support for their work on low-cost computerized physical therapy games (Sadeghi et al., 2017). Unlike generic computer games, these specialized games promote scientifically proven physical motions to aid people with disabilities (Corti et al., 2018). Unlike generic computer games, these specialized games promote scientifically proven physical motions to aid people with disabilities (Sadeghi et al., 2017). Goals, challenges/missions, incentive systems, personalisation, and 3D settings are employed to foster adherence (Domen et al.,

2019). Patients were taught unsupervised at home to evaluate stand-alone CT feasibility, with only reactive aid supplied when needed (Sadeghi et al., 2017).

Chapter 7

Discussion

Around 27 Parkinson's disease is caused by a variety of variables, and these factors may or may not be the major cause of Parkinson's disease (Llorca et al., 2016). In the early stages of Parkinson's, symptoms are minor and vary across individuals. Moreover, symptoms include muscle stiffness, poor balance, abnormalities in writing and speaking, and memory issue (He et al., 2018). However, the doctors took measures to reduce the symptoms. They try to keep dopamine levels right. Inhibitors of MAO-B and COMT are among the drugs used to treat Parkinson's disease. Sedentism is linked to PD. One research found that sedentism did not enhance Parkinson's risk (Uyar & Yildiran, 2019). While the specific causation of Parkinson's disease is unknown, various environmental and lifestyle variables have been linked to the condition (Kalia & Lang, 2015). "Sedentary behavior characterized by extended sitting has been related to increase overall morbidity and mortality regardless of the amount of time spent on physical activity," the researchers said. "As a consequence, sedentary behavior might impact PD pathogenesis in ways other than physical activity". A healthy lifestyle, on the other hand, may decrease the course of Parkinson's disease (Hoehn & Yahr, 1967). In this case, it's essential to have a healthy diet, eat nutritious meals, and consume the right amount of calories. Physical activity may also help to slow down the course of Parkinson's disease (Kalia & Lang, 2015). According to a systematic analysis, men who do not engage in physical exercise have a greater chance of having Parkinson's disease at some time in their life. Importantly, the trials showed that even little exercise may mitigate this effect. Stress management and mind-body practice are also important in slowing the course of Parkinson's disease since they assist to prevent sadness, anxiety, various types of hallucinations and nerve damage (Kalia & Lang, 2015). However, the majority of individuals are unaware that leading a healthy lifestyle will help them avoid not just PD. Also, it is very unfortunate that enough research has not yet been available

with Parkinson's disease lifestyle. More study will help us understand the cost-effectiveness of treating Parkinson's disease and other neurodegenerative diseases. Parkinson's disease research needs additional randomized trials.

Chapter 8

Conclusion

The research of a healthy lifestyle for Parkinson's disease has made significant progress. We are quite concerned since there is no conventional therapy for Parkinson's disease. Parkinson's disease therapy is tailored to each patient's unique set of symptoms. There are two alternatives for treatment: medication and surgery. As a result, lifestyle changes such as getting more sleep and engaging in physical activity have been shown to slow the advancement of the disease. Parkinson's disease should be made more widely known and a cure should be found. Disease-modifying medicines with neuroprotective effects are expected to take center stage in Parkinson's disease research in the near future. Rehabilitative exercise can enhance mobility, quality of life and balance in Parkinson's disease patients. These healthy habits can help slow the progression of Parkinson's disease. For those with Parkinson's disease, it is imperative to keep a healthy body and mind since regular exercise is essential for relieving muscle stiffness and tension. As a result, we may intervene early in the disease and slow down its course by adopting a balanced diet and exercise routine.

Chapter 9

Challenges and Future Perspectives

Living with Parkinson's disease is difficult because of the progressive loss of motor function, as well as a variety of other non-motor symptoms, that occur as a consequence of the disease's degenerative nature (Uttekar, 2021). As the second most common neurological ailment, Parkinson's disease (PD) is often undermined. Most significantly, the majority of people are unaware that leading a healthy lifestyle may protect them not just from developing Parkinson's disease but also from a host of other potentially fatal conditions (Uttekar, 2021). Similarly, medical treatments for Parkinson's disease are limited. Additionally, there are few resources available from which we may understand how a healthy lifestyle might help prevent the progression of PD. People with Parkinson's disease may reduce their risk of developing the disease's symptoms in the future by following a regular daily schedule and eating a healthy, balanced diet. In addition to medical therapy, the physician should recommend a fundamental healthy lifestyle to PD patients. Researchers are also doing study on these concerns, and it is believed that in the future, this will open the door to an infinite number of alternatives for reducing the cause of Parkinson's disease.

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