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## Parkinson's Disease: Current Treatment Options

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Parkinson's Disease: Current Treatment Options

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## Abstract

Parkinson's Disease is a neurodegenerative disease that is caused by a lack of dopamine. This lack of dopamine has many effects on a person's body who has Parkinson's Disease including loss of motor control, slowed movement (bradykinesia), changes in speech, impaired posture and balance, and muscle rigidity. The object of this paper is to explore some of the many different options for treatment of symptoms of Parkinson's Disease that are currently available. There is not one over-arching treatment that can alleviate the symptoms that are caused by Parkinson's Disease. However, if multiple treatments are used together, a patient who is diagnosed with Parkinson's Disease can live their life with not as strong symptoms and are able to regain their freedom that this disease has taken from them.

One sentence summary: This paper explores a few of the many different pharmacological and non-pharmacological treatment options for Parkinson's Disease.

## Causes of Parkinson's Disease

Parkinson's Disease is an increasingly common neurodegenerative disease that currently has no cure. It is very common in cases where Parkinson's has been diagnosed to see depigmentation of the substantia nigra. This depigmentation is thought to be present due to the progressive and degenerative loss of dopaminergic neurons and receptors. In this depigmented substantia nigra, there also seems to be the presence of intraneuronal inclusions called Lewy bodies.<sup>1</sup> These Lewy bodies are commonly found in the surviving neurons that haven't been degraded yet. Lewy bodies are enriched in one of the main genes thought to be the cause of Parkinson's,  $\alpha$ -synuclein, as well as many other proteins that have been ubiquitinated and await destruction.<sup>2</sup> Due to the mutations in these genes and other accompanying manifestations, about 50% of the neurons in the substantia nigra are degraded and rendered useless. This causes a depletion of dopamine within the striatum, which leads to a loss of control of the motor circuits of the body, resulting in the clinical causes of Parkinson's that are most common in someone who is afflicted. The clinical signs that are most common in someone who has Parkinson's Disease is muscular rigidity, slowness of movement, postural instability, and the most famous

Locus	MOI	Gene (protein)	Protein function	Clinical presentation	Neuropathology	Age at onset
PARK1 (PARK4)	AD	SNCA ( $\alpha$ -synuclein)	Unknown synaptic function	Duplications: Idiopathic PD; some postural tremor; slow progression	LBs	Mid 30–mid 60
				Triplications: PD; PD with dementia; diffuse LBs disease; aggressive course		LBs and LNs; $\pm$ glial inclusions; hippocampal CA2 and CA3 loss
				Mutations A53T, A30P, E46K: Idiopathic PD; parkinsonism and diffuse LBs	LBs and LNs; $\pm$ tau inclusions; amyloid plaques	30–60
PARK2	AR	Parkin	E3 ubiquitin ligase	Parkinsonism; slow progression	Variable presence of LBs	Juvenile to 40
PARK5	AD	UCHL1	Ubiquitin hydrolase and ligase	PD	Unknown	30–50
PARK6	AR	PINK1	Mitochondrial Ser–Thr kinase	Parkinsonism	Unknown	30–50
PARK7	AR	DJ-1	Oxidative stress response?	Parkinsonism	Unknown	20–40
PARK8	AD	LRRK2 (dardarin)	Unknown protein kinase	PD	Diffuse LBs; LNs; $\pm$ tau inclusions; $\pm$ amyloid plaques	40–60

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; LBs, Lewy bodies; LNs, Lewy neurites; MOI, mode of inheritance; OE, overexpressed; PD, Parkinson's disease.

Figure 1. Different genes and their suggested relationships to Parkinson's Disease.

one, the resting tremor. Through research and diagnostic testing, it has been found that there are multiple potential causes for someone being diagnosed with Parkinson's. Most cases are thought to be sporadic, but there are multiple genes that have been targeted for study that when mutated, give rise to common and familial forms of Parkinson's. The main genes that are currently being focused on are  $\alpha$ -synuclein (SNCA), parkin, leucine-rich repeat kinase 2 (LRRK2), PTEN-induced putative kinase 1 (PINK1), and DJ-1.<sup>3</sup> Figure 1 above shows the different genes that could have a relationship with causing Parkinson's Disease, their suggested functions, and reasons they are thought to be the causes for Parkinson's Disease. SNCA and LRRK2 both are autosomal dominant genes that are thought to be causes of this disease.<sup>4</sup> They are thought to be affected through a gain-of-function mutation or a dominant negative effect mutation on the

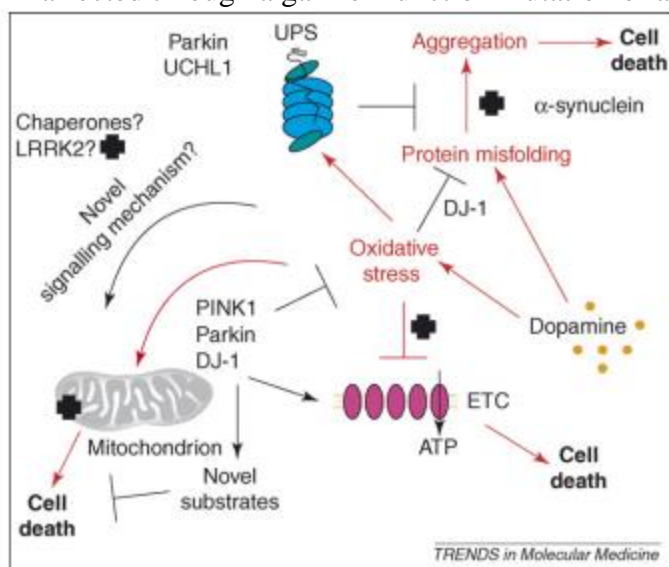


Figure 2. Concept map of how different genes related to Parkinson's disease interact.

protein.<sup>5</sup> Parkin, PINK1, and DJ-1 are all autosomal recessive genes that when mutated, can have different functions than normal and can cause some of the effects that lead to Parkinson's Disease.<sup>6</sup> Figure 2 to the left is a concept map of how these different genes and proteins all link together and how their functions all can depend on each other. While each case of Parkinson's

is different, being able to narrow to the exact cause of why someone is afflicted with this disease is key in being able to treat this disease. There are different treatment options available for people diagnosed with Parkinson's Disease, some medicinal and some non-medicinal. Different

routes of treatment, pharmacological and non-pharmacological, for Parkinson's Disease, will be discussed in this paper.

#### Current Parkinson's Disease Treatment Options – Non-Pharmacological

Parkinson's Disease is a crippling neurodegenerative disease that affects many aspects of day to day life. While there are treatments to help aid with the symptoms that accompany this disease, there is no cure for Parkinson's at this current time. However, there are a few different routes of treatment that patients can explore to help slow down the degeneration of motor skills and can help people living with Parkinson's Disease. Montgomery claims in his review of rehabilitative approaches to Parkinson's that there are multiple avenues and therapy options for people dealing with Parkinson's, such as physical therapy, occupational therapy, and speech therapy.<sup>7</sup> He also says that these therapy options are hopefully being used to directly modify the physiological processes in the brain, so people dealing with Parkinson's can overcome the symptoms that Parkinson's causes. In one research article, one of the biggest therapy strategies that Montgomery talks about is helping people with Parkinson's manage their symptoms using neurophysiological support. Using this kind of support can help patients conceptualize their difficulties and alter their expectations to be able to achieve more reasonable goals and to relearn how to do basic tasks, if needed.<sup>7</sup>

Movement impairments related to Parkinson's Disease are especially difficult for almost all patients that are showing symptoms. Some of these movement impairments relate to maintaining balance while standing, losing postural stability, difficulty doing simple tasks that affect daily living, and frequent falls. While some of the motor ailments of Parkinson's can be treated medicinally, not all of them can be treated using drugs. There are other ways to help treat this disease and one of them is physical activity. Physical activity has been shown to slow down

the deterioration of motor functions in the body and help to prolong functional independence.<sup>8</sup> Even after the introduction of drugs such as Levodopa, which is primarily used to treat Parkinson's Disease, many doctors believed that if paired with physical activity, can help maximize the benefits of the medication.<sup>9</sup>

One of the biggest non-medicinal treatment options for people with Parkinson's is physical therapy. In physical therapy for Parkinson's patients, one of the most basic styles of therapy is amplitude training. According to the John Hopkins Medicine official website, during this kind of physical therapy, a specific form of physical therapy called LSVT training is used. LSVT BIG stands for Lee Silverman Voice Treatment, and BIG stands for big movements. In this treatment option, patients make large and overexaggerated physical movements based on what their physical therapist says, like swinging their arms or taking really high steps. Doing these overexaggerated movements is thought to help retrain the muscle to do basic movements and to help slow down the progression of hypokinesia.<sup>10</sup> Another form of physical therapy that can help people with Parkinson's feel more confident with living day-to-day is reciprocal pattern therapy. This form of therapy is thought to help reinforce just basic movements that become hard or impossible with Parkinson's. Some of these reciprocal behaviors are sometimes as simple as swinging the arms when walking or taking basic steps in front of one another while walking. Doing these simple behaviors over and over is thought to relearn the basic movements and ingrain how to do them while dealing with the symptoms of Parkinson's.<sup>10</sup> One aspect of life that Parkinson's Disease disrupts is normal balance. The disruption of balance in everyday life can have a major impact on people with Parkinson's. Balance is a combination of visual feedback from a certain stimulus, the balancing system in the inner ear reacting to said stimulus, and then the brain interpreting these two feedback mechanisms together. Balance therapy has shown in



**Table 2. Study Measures at Baseline and 6 Months and Between-Group Differences in the Change from Baseline.<sup>a</sup>**

Measure	Tai Chi (N=65)	Resistance (N=65)	Stretching (N=65)	Between-Group Difference in Mean Change from Baseline <sup>†</sup>			
				Tai Chi vs. Resistance (95% CI)	P Value	Tai Chi vs. Stretching (95% CI)	P Value
<b>Maximum excursion (%)<sup>‡</sup></b>							
Baseline	64.05±16.60	64.02±18.53	64.35±17.22				
6 mo	73.62±13.44	68.03±18.48	61.94±16.39	5.55 (1.12 to 9.97)	0.01	11.98 (7.21 to 16.74)	<0.001
<b>Directional control (%)<sup>§</sup></b>							
Baseline	65.75±20.16	65.12±21.60	65.93±17.23				
6 mo	73.77±11.49	62.69±22.82	62.56±21.62	10.45 (3.89 to 17.00)	0.002	11.38 (5.50 to 17.27)	<0.001
<b>Stride length (cm)<sup>¶</sup></b>							
Baseline	115.6±19.7	114.5±21.1	115.7±18.6				
6 mo	125.9±20.3	118.8±20.7	113.6±18.5	5.9 (1.5 to 10.4)	0.01	12.3 (8.3 to 16.4)	<0.001
<b>Gait velocity (cm/sec)<sup>  </sup></b>							
Baseline	110.1±21.0	109.2±25.4	110.9±21.7				
6 mo	120.6±21.5	119.1±24.0	106.4±20.2	0.5 (-6.2 to 7.1)	NS	14.9 (9.8 to 20.1)	<0.001
<b>Peak torque knee extension (Nm)<sup>**</sup></b>							
Baseline	61.8±31.5	59.2±37.0	61.6±37.4				
6 mo	75.7±38.7	73.8±40.5	62.1±30.8	-0.6 (-10.8 to 9.5)	NS	13.5 (3.4 to 23.6)	0.01
<b>Peak torque knee flexion (Nm)<sup>**</sup></b>							
Baseline	32.6±19.1	29.1±17.0	32.6±18.4				
6 mo	37.7±19.3	38.0±18.2	30.0±17.9	-3.8 (-10.2 to 2.7)	NS	7.7 (1.9 to 13.6)	0.01
<b>Functional reach (cm)<sup>††</sup></b>							
Baseline	24.4±6.9	24.4±6.5	25.0±7.3				
6 mo	29.4±5.5	26.6±6.5	25.0±7.3	2.8 (0.6 to 5.0)	0.01	4.9 (3.0 to 6.9)	<0.001
<b>Timed up and go (sec)<sup>‡‡</sup></b>							
Baseline	8.60±2.90	8.95±2.72	8.69±3.18				
6 mo	7.55±2.69	7.95±2.60	8.67±3.45	-0.05 (-0.55 to 0.46)	NS	-1.03 (-1.58 to -0.47)	<0.001
<b>UPDRS III score<sup>§§</sup></b>							
Baseline	15.28±5.59	15.32±6.04	15.06±6.17				
6 mo	8.86±4.12	10.25±4.83	13.66±7.54	-1.34 (-3.28 to 0.59)	NS	-5.02 (-6.90 to -3.13)	<0.001

\* Plus-minus values are means ±SD. NS denotes not significant. A more detailed version of the table, including results from the 3-month postintervention follow-up, is available in the Supplementary Appendix.

† Mixed repeated-measures analysis of variance (group by time) with baseline, 3-month, and 6-month values indicated a significant between-group difference across all outcome measures (range, P=0.006 to P<0.001). Analyses were performed on an intention-to-treat basis. Point estimates and estimates falling within the 95% confidence interval were generated from independent t-tests for group differences. (See also Fig. 1 in the Supplementary Appendix.)

‡ Maximum excursion was assessed as the farthest distance displaced by the participant's center of gravity during performance of leaning and reaching tasks. Scores range from 0 to 100%, with higher percentages indicating better balance.

§ Directional control was assessed as the amount of movement toward a target, as compared with extraneous movement (away from the target), defined as the ratio of the amount of intended movement minus the amount of extraneous movement, divided by the amount of intended movement. The composite score of eight directions was used for analyses. Scores range from 0 to 100%, with higher percentages indicating better movement control.

¶ Stride length was measured as the distance between the heel points of two consecutive footprints of the same foot. Higher scores indicate greater stride length.

|| Gait velocity was measured by dividing the distance traveled by the ambulation time. Higher scores indicate greater gait velocity.

\*\* Peak torque was measured at an angular velocity of 60 degrees per second. Values are given in Newton meters (Nm). Results were the average of five repetitions of measurements at both limbs, with higher values indicating greater strength.

†† Functional reach was assessed as the maximal distance a participant could reach forward beyond arm's length while maintaining a fixed base of support in a standing position. Higher scores indicate better balance.

‡‡ Timed up and go was measured as the time taken to rise from a chair, walk 3.1 m (10 ft), return, and sit down. Higher scores indicate better mobility.

§§ The 14-item motor section of the Unified Parkinson's Disease Rating Scale (UPDRS) III was scored on a 5-point Likert scale from 0 to 4, with 0 representing no impairment and 4 representing marked impairment. Lower values indicate less motor disability. A change of 5 points or more in the score is considered clinically meaningful.<sup>31</sup>

Figure 3. Data from Tai-Chi study at baseline and six months for the different groups.

different studies to be an exceptional tool for people with Parkinson's and in turn, helping the patients regain their confidence in living with their condition. In this therapy style, practice balancing and walking in straight lines is done. During these therapy sessions, the patient is taught how to compensate for changes in their balance.<sup>10</sup> Studies have shown that patients who use this type of physical therapy have increased confidence in performing simple tasks, such as walking and sitting in a chair, which can help the patient to be more secure living with this disease. One unique way that people with Parkinson's Disease can help keep their balance and posture strong is to engage in Tai Chi! In a study published in the New England Journal of Medicine, Tai Chi was shown to "improve strength, balance, physical function, and to prevent falls in older adults".<sup>11</sup> In the Tai-Chi study, there were 3 groups of participants. All participants of the trial had Parkinson's Disease. They were broken up into different groups; one group that would be participating in Tai Chi for their physical activity/therapy, one group that would be

different studies to be an exceptional tool for people with Parkinson's and in turn, helping the patients regain their confidence in living with their condition. In this therapy style, practice balancing and walking in straight lines is done. During these therapy sessions, the patient is taught how to compensate for changes in their balance.<sup>10</sup> Studies have shown that patients who use this type of physical therapy have increased confidence in performing simple tasks, such as walking and sitting in a chair, which can help the patient to be more secure living with this

doing Resistance training, and the last group that would be doing Stretching. Tai Chi was found to help reduce balance impairments, as well as add additional benefits to improved functional capacity and reduced falls, when compared to the other groups.<sup>11</sup> Figure 3 above shows data and statistics for the three different trial groups. For most of the data, there seems to be a significant difference between Tai Chi and Resistance groups for some changes from the baseline in maximum excursion, directional control, and stride length. However, there is a significant difference between Tai Chi and Stretching groups in every category in the table. The significant difference between the Tai Chi group data and the Resistance and Stretching group data showed that Tai Chi was more effective at treating and empowering different basic functions for people dealing with Parkinson's. One of the biggest problems with Parkinson's Disease is a patient

being unable to control their motor movements and falling, which can cause significant damage. Falling is

<b>Falls</b>	<b>Tai Chi (N = 65)</b>	<b>Resistance (N = 65)</b>	<b>Stretching (N = 65)</b>
Total falls <sup>†</sup>	62	133	186
No. of falls — no. of participants (%)			
Any	19 (29)	31 (48)	26 (40)
1	3 (5)	8 (12)	4 (6)
2	4 (6)	7 (11)	2 (3)
≥3	12 (18)	16 (25)	20 (31)
Rate — no./participant-month	0.22	0.51	0.62

Figure 4. Data from Tai-Chi study regarding the amount of falls each group had during the study.

a significant part of dealing and living with Parkinson's due to the affected individual's balance being diminished. One of the purposes of this research study was to look at the adverse effects of daily living and falls that participants were involved in, depending on what group of they were in. Figure 4 above shows data collected from participants regarding how many total falls they had while participating in this study. This data shows that the group that participated in Tai Chi had a significantly lower number of falls than the participants in the Resistance group and the

Stretching group. Focusing on more strenuous physical therapy options, if the patient is able to, that help to reduce the number of falls and relieve other negative side effects in the life of someone with Parkinson's might be a key non-medicinal treatment route. This study's results show that there are many unique and different ways for people living with Parkinson's to strengthen their motor control, even though they have a degenerative disease. One final physical therapy strategy that is good for people living with Parkinson's is basic strength training. While muscles weaken naturally as someone gets older, these effects are multiplied in patients with Parkinson's. Doing strength training such as resistance exercises with light dumbbells or a resistance band can help the patient maintain positive motor control over their muscles. Pool-based strength training classes are also great for people living with Parkinson's because it helps to take the excess force off of joints and muscles, while also training and using them in an efficient manner.<sup>10</sup>

One of the most important parts of battling with any disease is the mental and physiological aspect. If someone is diagnosed with a disease or a condition and they are defeated in their minds and they have no hope of ever getting better, then the disease has already won.<sup>12</sup> However, if the person that was diagnosed stays positive about their outcome and truly believes they can beat their condition, then their outlook on life and dealing with treatment stays high. Many diseases and conditions have support groups where people who are afflicted by said disease or condition, can go and talk to and support one another, and Parkinson's Disease is no different. Parkinson's Disease is a crippling disease that deteriorates their physical and mental condition. People with Parkinson's will eventually lose their ability to live life on their own and will no longer be able to control their lives or bodies. However, it has been shown that when patients have access to professional or member-led support groups, the acceptance for the disease

goes up and patients are better able to cope with its challenges.<sup>12</sup> Support groups of any kind are also another important part of therapy and learning to live with the disease. Online support groups are becoming ever more popular with recent technological advancements.<sup>13</sup> Online support groups also help people with Parkinson's because it gives them easy access to help and support, without having to leave the comfort of their home.<sup>14</sup> In Attard's journal, she looked at how accessing support forums and groups can have a positive impact on people dealing with disease, especially Parkinson's Disease. On these forums and online support groups, people were able to offer much valued support and advice, especially during times of crisis or great emotional distress. One quote from the forum states that, "the importance of the forums as a source of support was apparent as members often expressed their gratitude towards other for informing, encouraging, caring, and thinking of them as they battles with the disease".<sup>12</sup> One strength of support groups and online forums is that people who have been diagnosed with the disease for a longer period of time than others can help guide and share experiences with people who have been recently diagnose. Attard stated that sharing personal stories was an integral part of the support groups and forums. The forums and groups also allowed people to stay connected and up to date on interesting and useful information, as well as keeping up with the latest advances in medication/treatment. One of the most important parts of support groups and online forums is helping an inflicted individual see that they are not alone in their fight. Attard states that new members to the online forum often felt relief when they finally realized that there were other people struggling with the same day to day experiences that they were and that they were not alone. One final important note about support groups and online forums is that they are an incredible tool to help people with that disease to stay encouraged and have positive thinking.<sup>15</sup> Attard states that a number of members would post on the online forum about how they were

determined to live a full life and not let their disease or illness dominate their lives.. Being able to gain insight from others and to have support on the bad days is just as important as important as keeping up with a physical therapy regiment. Mental/emotional therapy can help to strengthen the mind and keep the spirits up while dealing with a debilitating disease.<sup>16</sup>

### Current Parkinson's Disease Treatment Options – Pharmacological

Being able to relieve some of the effects of degenerative diseases is key for patients to be able to live a mostly normal life. Drugs that can inhibit certain receptors, make missing substances out of precursors, and slow down the negative effects of a disease are all important. Most disease have some sort of medical treatment available and Parkinson's Disease is no different. One of the most famous drugs used to treat Parkinson's is Levodopa. In Parkinson's Disease, the cause of the symptoms is due to a decrease in dopamine production.<sup>17</sup> More specifically, degradation of the substantia nigra occurs and this leads to massive disruption in the brain's nigrostriatal pathway. This leads to one of the common signs of Parkinson's Disease, a decrease in production of dopamine. Levodopa helps to fill the body's missing dopamine levels by administering the precursor so the body can change it into the usable form of dopamine easily. Levodopa is very efficient because it can cross the blood-brain-barrier, while regular dopamine cannot. Levodopa is commonly taken with carbidopa, which is a dopamine decarboxylase inhibitor. The main reason carbidopa is commonly taken along with Levodopa is because carbidopa can decrease the amount of levodopa that is converted into dopamine in the periphery, so levodopa can cross the blood-brain-barrier and be more effective. Once levodopa has crossed the blood-brain-barrier, it is converted into dopamine. This dopamine that is produced helps to activate postsynaptic dopaminergic receptors in the brain, which help to

compensate for the natural decreased dopamine production.<sup>18</sup> It is most commonly used to treat Parkinson's and is usually prescribed once the patient's symptoms become too severe.

Even as powerful as a drug that Levodopa is, its bioavailability is something to be concerned about. Its bioavailability when taken orally is only around 30%.<sup>19</sup> There has been thought that other methods of delivery of this dopamine precursor should be considered. One other route that is being explored is delivering Levodopa via an intranasal injection with nanoparticles. With this route, it is thought to bypass the blood-brain-barrier and peripheral metabolism totally, being delivered to the brain via the olfactory and trigeminal nerve pathways.<sup>20</sup> Even though this current route of treatment is thought to be more effective and easier to administer, it is still in the experimental phase, but it has shown promising results.<sup>19,20</sup>

Other than dopamine precursors, there exists another kind of drug used to treat Parkinson's Disease called dopamine agonists. There are currently 10 dopamine agonists that are marketed for the treatment of Parkinson's. Five of these dopamine agonists are ergot derivatives, meaning they are derived from a fungus that produces alkaloids called ergotamines. These 5 drugs are bromocriptine, cabergoline, dihydroergocryptine, lisuride, and pergolide. The other 5 dopamine agonists are non-ergot derivatives, and they are apomorphine, piribedil, pramipexole, ropinirole, and rotigotine.<sup>25</sup> The most popular choice among these dopamine precursors is pramipexole. When discussing medicinal treatments for Parkinson's Disease, it is important to understand that different drugs may have different impacts on different people. There is not one single treatment option that covers all angles of Parkinson's, and most times, multiple of these drugs are used together to help treat symptoms. It is important to look at each patient as an individual and to devise the proper treatment plan for them, and not go off of what worked in the treatment of someone else.

One commonly seen drug that is used to treatment the symptoms of Parkinson's Disease is Pramipexole. Even though Levodopa is seen as the "golden standard" drug for treating Parkinson's, in recent years, its effectiveness has faded quickly for some patients and it has been known to cause extreme motor fluctuations as well.<sup>21</sup> Pramipexole is a dopamine agonist, unlike levodopa, which is a dopamine precursor. Pramipexole is a non-ergot D2/D3 synthetic aminobenzothiazole derivative that is found to be an effective monotherapy is patients that have been recently diagnosed with Parkinson's Disease.<sup>22</sup> Pramipexole, when taken, has selective affinity and action at dopamine receptors in the brain that belong to the D2 subfamily. When pramipexole is bound to these receptors, it is seen to have full activity similar to if sufficient levels of dopamine were present. With this specific drug activating dopamine receptors, instead of making dopamine like levodopa, it has shown been shown to not cause as severe muscle and motor fluctuations in patients.<sup>23</sup> One other dopamine agonist that has seen wide usage to treat Parkinson's Disease is ropinirole. Ropinirole was widely accepted as a transdermal patch delivery to help treat early Parkinson's, but it has been withdrawn from the US markets, due to the drug crystalizing in the patch.<sup>24</sup>

In the table below, there is a comparison for levodopa vs dopamine agonists in the treatment for Parkinson's Disease. While both drugs have the potential to show possible neurotoxic or neuroprotective effects in vitro, both drugs have strong evidence of no neurotoxic or neuroprotective effects in patients with Parkinson's disease.<sup>26</sup> Levodopa has shown to provide better motor efficacy in the early years after diagnosis and treatment has begun, but the side effects of levodopa have been shown to be at an increased level as well. Levodopa is shown to have more motor fluctuations and have earlier onset dyskinesia than dopamine agonists. While the dopamine agonists do not have as severe side effects of levodopa, the motor efficacy is lower

in patients that take this drug over levodopa.<sup>27</sup> Overall, both drugs are extremely effective at improving the quality of life of someone that has Parkinson's Disease.<sup>25</sup>

	Levodopa	Dopamine Agonists
Neurotoxic or Neuroprotective effects	<i>In-vitro</i> : high dose: toxic low dose: possible protective <i>in vivo</i> or PD patients: no evidence of either toxic or protective effects	<i>In-vitro</i> or <i>in-vivo</i> : Possible protective effects <u>In PD patients</u> : No evidence of protective effects
Early PD: Initial treatment		
<i>Short-term outcomes (3-5 years)</i>	More motor fluctuations and dyskinesias	Less motor fluctuations and dyskinesias
	Earlier onset of dyskinesias	Delayed onset of dyskinesias
	Better motor efficacy	Lower motor efficacy
<i>Long-term outcomes (&gt;5 years)</i>	Similar prevalence of motor fluctuations and dyskinesias	
	Better motor efficacy	Lower motor efficacy
Advanced PD: CDC choices	Both improve quality of life, motor dysfunction and motor complications.	
	Greater improvement in NMSS total score	Greater improvement in mood and apathy scores of NMSS
Side-effects	More motor complications	More non-motor side-effects

Table 5. Levodopa vs Dopamine Agonists.<sup>25</sup>

One interesting side effect of Parkinson's Disease is psychotic symptoms that become prevalent due to the continuum of Parkinson's Disease progression. The National Institute of Neurological Disorders and Stroke and National Institute of Mental Health use the term "PD psychosis" (PDP) to describe these symptoms.<sup>28</sup> When dealing with PD psychosis, criteria for a correct diagnosis of psychosis caused by Parkinson's Disease must be met. These criteria are: (1) The presence of at least one of the following symptoms: illusions, false sense of presence, hallucinations, or delusions; (2) A diagnosis of Parkinson's Disease before any of the symptoms started to occur; (3) The symptoms are recurrent or continuous for at least 1 month; (4) The symptoms aren't better classified as another mental health disorder such as dementia, schizophrenia, delusional disorder, and mood disorders.<sup>29</sup> PDP may occur partially due to the medications that a patient is taking to treat their Parkinson's symptoms. These drugs include levodopa and dopamine agonists, which were both discussed above. Levodopa and dopamine



agonists are crucial drugs in helping to treat the symptoms of Parkinson's Disease and can not stop being administered. There have been different drug trials to try and find a solutions for these psychotic symptoms, and one medication has shown strong indications of being able to treat those symptoms. Pimavanserin, otherwise known as Nuplazid, is an atypical antipsychotic medication, and is also the first medication that has been approved by the FDA to help treat the symptoms of hallucinations and delusions associated with Parkinson's Disease psychosis.<sup>30</sup> One of the main reasons that this specific drug is effective at treating these symptoms is because it does not have affinity and lacks activity at dopaminergic, muscarinic, adrenergic, and histaminergic receptors, meaning it does not interact or block the treatment routes of levodopa and dopamine antagonists. It has also shown to not have any serious adverse side effects and does not worsen the motor symptoms of Parkinson's Disease.<sup>30</sup>

## Conclusion

Parkinson's Disease is a chronic and progressive neurodegenerative disorder that impairs motor function, presents bradykinesia, rigidity, and postural instability. This paper has explored different treatment options for patients that are currently available to treat the symptoms of Parkinson's Disease. While there is no cure for Parkinson's, a combination of pharmacological and non-pharmacological treatment methods is the best way to combat the symptoms that Parkinson's Disease shows. There is no one drug or physical therapy method that is the best option for treatment. Exploring different treatment routes and finding what is best for the patient should always be desired. I hope this paper has shown that there are different methods to treating Parkinson's Disease, and hopefully one day, a cure will be found to rid the world of this disease.

### Potential Future Work With Topic

Parkinson's Disease is a crippling disease that affects millions of people around the world, including some of my close and immediate family. In the future, I am planning on going to medical school and I think it would be very interesting to do research, if possible, for future drugs to help treat Parkinson's Disease, or even a cure for it. I plan on continuing my own research into different treatment methods and looking into up and coming drugs that could help to end this disease and staying educated on this topic.

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