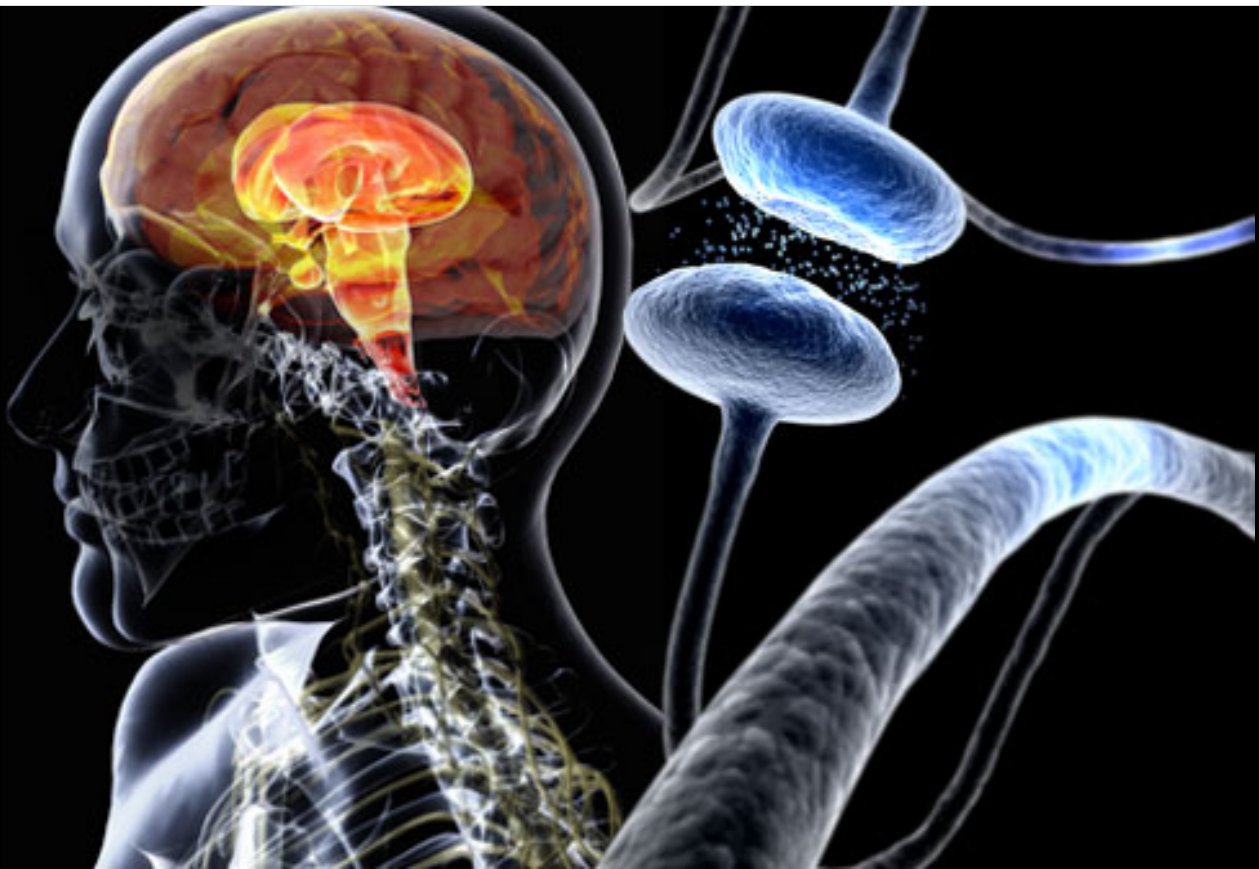




RAMBAM

Health Care Campus

Revolutionary New Treatment for Parkinson's Disease Tremors



Information Guide & Treatment Options

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1. Introduction

The Parkinson's Disease Foundation defines Parkinson's disease as "a chronic and progressive disorder that involves the malfunction and death of vital nerve cells in the brain called neurons." Parkinson's primarily affects neurons in an area of the brain called the *substantia nigra*. The Foundation estimates that approximately seven to 10 million people worldwide are living with Parkinson's disease.

The underlying cause of Parkinson's disease is not currently known. According to the National Institute of Health, "most cases of Parkinson's disease probably result from a complex interaction of environmental and genetic factors."¹ Medical professionals agree that the symptoms of Parkinson's disease are caused by the progressive deterioration of neurons that are responsible for dopamine production in the brain. According to WebMD, "Dopamine serves as a chemical messenger allowing communication between the *substantia nigra* and another area of the brain called the corpus striatum. This communication coordinates smooth and balanced muscle movement. A lack of dopamine results in abnormal nerve functioning, causing a loss in the ability to control body movements." When approximately 60 to 80% of the dopamine-producing cells are damaged, and do not produce enough dopamine, the motor symptoms of Parkinson's disease appear.²

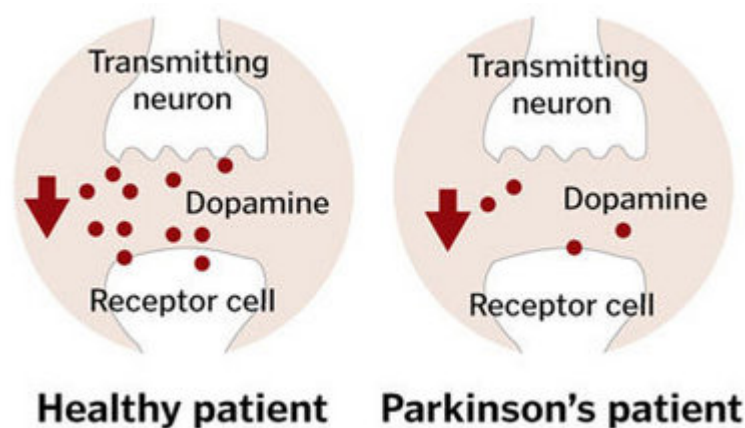


Illustration of dopamine production by a normal neuron as opposed to one affected by Parkinson's³

Parkinson's disease usually occurs in individuals who are over the age of 50. The Mayo Clinic states that Parkinson's "develops gradually, sometimes starting with a barely noticeable tremor in just one hand." The disease progressively worsens, leading to more pronounced and varied symptoms. Parkinson's disease primarily affects motor functions but can also affect emotional and cognitive abilities. Some

¹ National Institute of Health. *Parkinson's Disease*. Source: <http://ghr.nlm.nih.gov/condition/parkinson-disease>

² WebMD. *What Causes Parkinson's Disease?* Source: <http://www.webmd.com/parkinsons-disease/guide/parkinsons-causes>

³ Ibid

affected individuals develop psychiatric conditions such as depression and visual hallucinations. Individuals affected by Parkinson's also have an increased risk of developing dementia.⁴

Parkinson's disease is widespread, affecting individuals across all races and creeds in every single part of the globe. According to the National Institute of Health, Parkinson's disease occurs in approximately 13 individuals per 100,000. Since the risk of developing Parkinson's is associated with age, medical authorities expect the number of Parkinson's cases to increase as global life expectancy continues to grow in the coming decades.⁵

While Parkinson's disease is not fatal, it is, unfortunately, currently incurable. The nature of the disease renders affected individuals gradually incapable of completing everyday tasks and enjoying life due to the severity of some of its symptoms, such as mobility compromising tremors. Nonetheless, innovations in science and medicine have made Parkinson's significantly more manageable with the aid of a variety of medications and surgical procedures.⁶ New medical research innovations have led to groundbreaking developments in Parkinson's treatment, allowing for non-invasive, cost-effective, and time-sensitive surgical treatment with proven long-term results, instant symptom relief, and most importantly, an improved quality of life for affected patients.

2. Parkinson Disease Symptoms: Tremors

The Parkinson's Disease Foundation states that Parkinson's disease is characterizing by symptoms that inhibit motor skills due to decreases in dopamine production. Common symptoms include:⁷

- **Tremors** of the hands, arms, legs, jaw, and face
- **Bradykinesia** or slowness of movement
- **Rigidity** or stiffness of the limbs and trunk
- **Postural instability** or impaired balance and coordination

Symptoms of Parkinson's disease differ from person to person and can change as the disease progresses.

Tremors are the most recognizable and most common symptom of Parkinson's disease. Tremors are defined as "rhythmical, involuntary movements that affect a part of the body." Often, the first and most common symptom of Parkinson's disease is trembling or shaking of a limb, especially when the body is at rest. Typically, the tremor begins on one side of the body, usually in one hand. Tremors can also affect the arms, legs, feet, and face. As the disease progresses, tremors can spread to both sides of the body.

⁴ National Institute of Health. *Parkinson's Disease*. Source: <http://ghr.nlm.nih.gov/condition/parkinson-disease>

⁵ Ibid

⁶ The Mayo Clinic. *Parkinson's disease*. Source: <http://www.mayoclinic.org/diseases-conditions/parkinsons-disease/basics/definition/con-20028488>

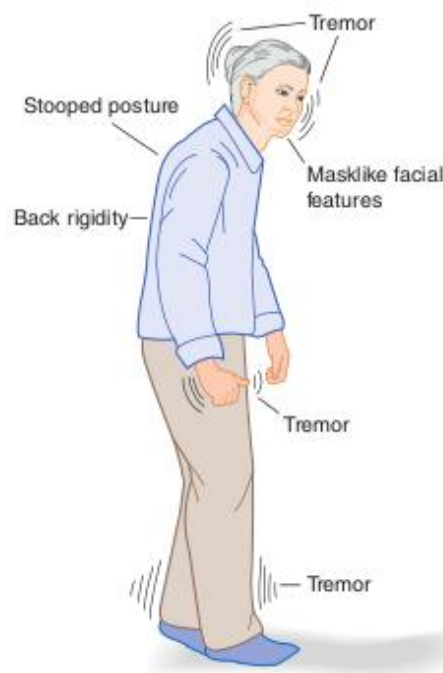
⁷ Parkinson's Disease Foundation. *What is Parkinson's Disease*. Source: www.pdf.org/about_pd

Emotional and physical stress tends to make the tremor more noticeable. Sleep, complete relaxation, and intentional movement or action usually reduce or stop the tremor.⁸

According to Parkinson's UK, a tremor caused by Parkinson's can appear in two ways:⁹

- A resting tremor might happen when the body is relaxed, for example when lying in bed
- An action tremor can happen when the body doing something, like trying to hold a magazine or drink from a cup

The Parkinson's Disease Foundation states that "in the early stages of the disease, about 70 percent of people experience a slight tremor in the hand or foot on one side of the body, or less commonly in the jaw or face. A typical onset is tremor in one finger." Typically, the fingers or hand will tremble when folded, or when the arm is held loosely at the side. The tremor usually ceases when a person begins an action. The tremor often spreads to the other side of the body as the disease progresses, but usually remains most apparent on the initially affected side.¹⁰ The most typical tremor in Parkinson's is called a 'pillrolling' rest tremor, as it looks like an affected individual is trying to roll a pill between their thumb and index finger.



Tremors are the most recognizable symptoms of Parkinson's disease¹¹

⁸ WebMD. *Parkinson's Disease – Symptoms*. Source: <http://www.webmd.com/parkinsons-disease/tc/parkinsons-disease-symptoms>

⁹ Parkinson's UK. *Tremor and Parkinson's*. Source: https://www.parkinsons.org.uk/sites/default/files/publications/download/english/fs94_tremorandparkinsons_0.pdf

¹⁰ Parkinson's Disease Foundation. *Primary Motor Symptoms*. Source: http://www.pdf.org/symptoms_primary

¹¹ Ibid

Parkinson's patients who suffer from tremors have a significantly lowered quality of life. The disease affects an individual's mobility and, as a result, their enjoyment of life and many of its activities. The tremors cause patients to become dependent upon others for care, losing their independence.

Beside tremors, Parkinson's patients suffer from the following symptoms:

- Stiff and aching muscles (often characterized by reduced arm swing)
- Slow, limited movements (especially when trying to move from a rested position)
- Weakness of face and throat muscles (patients may experience difficulty in swallowing and talking)
- Difficulty with walking and balance (characterized by a slight bend forward at the waist and other posture problems)
- Sudden brief inability to move (commonly referred to as 'freezing')



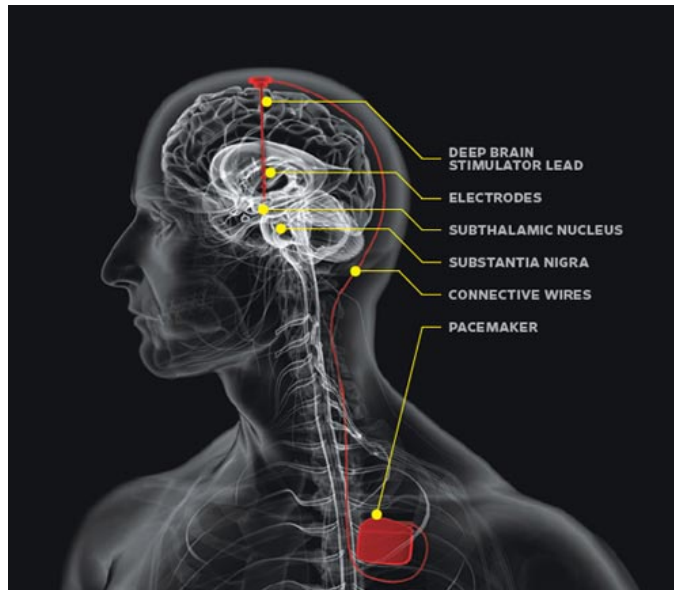
Illustration of the onset of Parkinson's balance and postural symptoms

3. Current Treatments for Parkinson's Disease

Current treatments for Parkinson's disease include prescription and surgical options. Treatment options include medication, such as Dopamine Agonists, Comt Inhibitors, Anticholinergics, and Amantadine. Prescription medication is primarily used to treat the less prominent Parkinson's symptoms, such as Bradykinesia, Rigidity, and Postural Instability. Levodopa is the most commonly prescribed drug for Parkinson's, as it can cross the blood-brain barrier and be converted to dopamine in the brain. Segeline, an MAO-B inhibitor, helps prevent the degradation of dopamine, allowing it to have a longer effect. Patients with Parkinson's can also be prescribed anticholinergic medications, which block nerve impulses that induce muscle movements. In severe cases of Parkinson's disease where patients either do not respond to drug therapy or face difficult side effects such as persistent tremors, surgical alternatives can be utilized. According to Brown University, potential surgical alternatives include Pallidotomy, thalamic stimulation, pallidal stimulation, and subthalamic DBS.¹²

¹² Brown University. DBS. Source:

http://biomed.brown.edu/Courses/BI108/BI108_2008_Groups/group07/Parkinsons.html



DBS uses a surgically implanted neurostimulator (powered by a pacemaker)¹³

The most popular surgical option for Parkinson's tremor treatment at the moment is Deep Brain Stimulation (DBS). DBS is a surgical procedure that blocks electrical signals from targeted areas in the brain. The procedure is currently only used for patients whose symptoms cannot be adequately controlled with medication. DBS uses a surgically implanted, battery-operated medical device called a neurostimulator which delivers electrical stimulation to targeted areas of the brain. DBS is a highly invasive surgical procedure that leads to mixed results. Most patients who undergo DBS still need to take medication after undergoing DBS. In addition, there is a 1-3% chance of infection, stroke, cranial bleeding, or other complications. Deep Brain Stimulation has been criticized by medical professionals as costly, requiring a prolonged recovery period, and not fully guaranteeing positive prognosis. A recent large-scale collective review of DBS found that "DBS is, on the one hand, an effective surgical treatment for movement disorders. On the other hand, it is a complication-prone operation. A dedicated 'Movement Disorder Team' consisting of neurologists, neurophysiologists, functional neurosurgeons, neuropsychologists and nursing specialists is essential. Liaison among team members in peri-operative periods and postoperative care is the key to avoiding complications and having a successful patient outcome."¹⁴

¹³ Chan DT, et al. *Complications of Deep Brain Stimulation – A Collective Review*. Asian Journal of Surgery. Oct 2009. 32(4). 285-63. Source: <http://www.ncbi.nlm.nih.gov/pubmed/19892631>

¹⁴ Ibid

4. Revolutionary New Treatment - Targeted Focused Ultra Sound (FUS)

Recently, a new revolutionary Parkinson's disease tremor treatment solution was developed by Israeli firm Insightec and has been implemented at the Rambam Medical Center. **Targeted Focused Ultra Sound (FUS) tremor Treatment** treats tremors through a non-invasive ablation of a tiny part of the brain, which serves as a relay station for transferring electrical signals. The purpose of the treatment is to allow Parkinson's patients to no longer experience painful and cumbersome symptoms, regain lost functions, and finally achieve the independence and efficiency they seek. The treatment is specifically intended for patients with primary tremor or patients with Parkinson's disease who suffer from tremors that cannot be controlled by medication and significantly disrupt the patient's quality of life and everyday function. The procedure is capable of treating full body, partial, and limb tremors. Candidates for the procedure should be able to undergo a long MRI scan and should not have any other active brain diseases or debilitating conditions that may intervene with treatment. Other conditions related to Parkinson's disease, such as stiffness, are not treated by FUS.



Patient undergoing non-invasive FUS treatment¹⁵

FUS tremor treatment has long-term effects and is theorized to last forever. The treatment is **non-invasive** and merely requires a 2 week visit with a 2 day hospitalization with 3 to 4 hours of non-invasive treatment procedures. During the treatment, the patient lies in an MRI machine. The MRI allows for the physician to examine the brain structure of the patient and define the treatment target area. The patient's head is secured to a special fixation frame that places the upper part of the patient's head in a helmet that administers the ultra sound waves. The physicians send focused ultra sound waves to the target area, in gradually increasing energy steps, while monitoring the patient's condition and adjusting the treatment correspondingly. The patient remains conscious during the treatment and is in constant communication with the physicians. The treatment lasts three to four hours, after which patients are placed on a 24 hour monitoring schedule during which primary studies of brain functions and additional MRIs are performed. Most patients demonstrate significant tremor improvement **immediately** after the

¹⁵ Focused Ultrasound Foundation. *Focused Ultrasound for Parkinson's Disease*. Source: <http://www.fusfoundation.org/>

treatment and continuous improvement in the months following treatment. Studies have shown that the treatment remains effective a year following the procedure and is expected to remain effective for the duration of the patient's life. There are no known severe side effects or dangers associated with FUS.

The treatment, which is exclusively offered at Rambam Medical Center, offers a number of key advantages over other treatments, such as Deep Brain Stimulation, including:

- Non-invasive procedure that has no need for skull incisions or brain implants
- Immediate and ongoing relief of tremors
- No permanent follow-up needed
- A reduced dependency on medications
- No damaging radiation
- Side effects, if any, are scarce and often appear only during the treatment itself
- Short treatment duration and two week follow-up result in less financial and emotional strain

5. Treatment in Rambam Medical Center's International Medicine Department – Haifa, Israel

Rambam is the largest hospital in Israel's Northern region and leads the country in the provision of health services to foreign patients through its International Medicine Department. The department offers the latest in all modern and technologically advanced medical procedures. Thousands of patients from all over the world apply online to the International Medicine Department each year. Patients visit Rambam for a wide variety of treatments and consultation provided by some of Rambam Medical Center's, and the world's, top specialist.

The innovative Targeted Focused Ultra Sound (FUS) Parkinson's treatment is offered to patients of Rambam's International Medicine Department as well as for the local population.



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