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Parkinson's Disease: A Concise Overview of Etiology, Epidemiology, Diagnosis, Comorbidity and Management

Getinet Ayano*

Research and Training Department, Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia

***Corresponding author:** Getinet Ayano, Research and Training Department, Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia, Tel: +251- 9-27-17-29-68; E-mail: ayanogetinet@yahoo.com

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Background

Parkinson's disease is a progressive neurodegenerative disorder that is associated with the loss of dopaminergic neurons in the substantia nigra pars compacta (SNc) [1]. It is a degenerative disorder of the central nervous system that belongs to a group of conditions called movement disorders. It is both chronic, meaning it persists over a long period of time, and progressive, meaning its symptoms grow worse over time. As nerve cells (neurons) in parts of the brain become impaired or die, people may begin to notice problems with movement, tremor, stiffness in the limbs or the trunk of the body, or impaired balance. As these symptoms become more pronounced, people may have difficulty walking, talking, or completing other simple tasks [2].

Patients with Parkinson's disease (PD) suffer from a severe loss of dopamine in the substantia nigra pars compacta (SNc), leading to disrupted basal ganglia function and to a loss ofmotor control [3]. The hallmarks of the disease are its triad of motor features—resting tremor, rigidity, and akinesia/bradykinesia (inability to initiate movement and slowness of movement, respectively). Gait and postural disturbances also characterize the disease. Parkinsonism, or parkinsonian syndromes, refers to the clinical appearance of Parkinson's disease without implying causation. Some patients, for instance, have parkinsonism secondary to antidopaminergic drugs, without pathology of the substantia nigra. Non-motor symptoms, however, are frequent impairments in PD and result in a major impact on the patients and their caregivers [1,4-6].

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease, and it affects over 1 percent of the population over age 55 and nearly 3 percent of the population over age [7,8].

Psychiatric disturbances affect up to 90 percent of patients at some point during the course of Parkinson's disease, and more than one psychiatric disturbance is often present. Early in the disease process, adult-onset anxiety and depressive disorders precede the obvious onset of motor symptoms in up to 30 percent of patients [9].

Treatment of Parkinson's disease requires an integration of medical, complementary and supportive therapies inputs, such as rehabilitations, diet, exercise, yoga, massage therapy, acupuncture, hypnosis, swallowing evaluation and speech therapy [10-18].

Etiology of Parkinson's Disease

Research has identified several factors that contribute to the risk of developing Parkinson's disease. It is a disease caused by biopsychosocial influences including genetic, nutritional, neuroanatomic, neurochemical and other biologic abnormalities. In addition psychological and socioenvironmental factors may increase the risk of Parkinson's disease. Increased age is associated with a greater risk of developing Parkinson's disease [19-25].

Genetic factors

Evidences identified that around 15% of individuals with Parkinson's disease (PD) have a first-degree relative who has the disease [23]. At least 5% of people are now known to have forms of the disease that occur because of a mutation of one of several specific genes [26]. Scientists identified that mutations in specific genes have been conclusively shown to cause Parkinson's disease (PD). These genes code for alpha-synuclein (SNCA), parkin (PRKN), leucine-rich repeat kinase 2 (LRRK2 or dardarin), PTEN-induced putative kinase 1 (PINK1), DJ-1 and ATP13A2 [25,26]. In most cases, people with these mutations will develop PD. With the exception of LRRK2, however, they account for only a small minority of cases of Parkinson's disease (PD) [25,27].

According to different studies several genetic mutations associated with PD, including the alpha synuclein gene, and many more genes have been tentatively linked to the disorder [25,26,28]. Mutation in LRRK2 is a common cause of Parkinson's disease (PD) [29]. The mechanism of LRRK2 in PD pathogenesis remains unclear; however, the most common disease-associated mutation in LRRK2, G2019S, shows higher kinase activity than wild-type. Therefore, over activation of LRRK2 kinase activity might be associated with disease pathogenesis [30].

Studies of large family and twin samples with heritable parkinsonian conditions have led to the identification of several causative genes as well as genetic variants that increase the risk for sporadic Parkinson's disease. One of the most prevalent genes associated with familial and sporadic Parkinson's disease is leucine-rich repeat kinase 2 (LRRK2). The locus for LRRK2, called PARK8, is located on chromosome 12q12. Its most common pathogenic mutation, G2019S, is found in up to 5 percent of Caucasian patients with familial Parkinson's disease. In Ashkenazi Jews and African Arabs, G2019S mutations are present in up to 30 percent of familial Parkinson's disease cases and 13 to 40 percent of sporadic Parkinson's disease cases. The G2385R LRRK2 variant is the most common genetic risk factor identified among Asian peoples, accounting for 23 percent of familial cases as well as 4 to 9 percent of early and typical late-onset cases. The physiological function of the LRRK2 protein remains unknown [24-29].

The α-synuclein gene (SNCA) mutation, located on chromosome 4q21–q23, was the first mutation identified in association with autosomal dominant Parkinson's disease. Although SNCA mutations are a rare cause of Parkinson's disease, the study of α-synuclein led to the discovery that it is a major component of Lewy bodies and demonstrated the role of protein aggregation in the pathophysiology of

Parkinson's disease. Because patients with sporadic Parkinson's disease, who have normal α-synuclein genes, have Lewy bodies that stain positive for α-synuclein and ubiquitin, it is possible that neuronal cell death in Parkinson's disease is related to abnormal accumulations of these proteins. Mutations in a gene on chromosome 6 that codes for Parkin (PRKN), a protein involved in the ubiquitination pathway, are the most common inherited defects and are particularly associated with a juvenile autosomal recessive form of early onset Parkinson's disease. Gene loci on chromosome 4 that affect ubiquitin processing (UCH-L1) are also linked to Parkinson's disease. Other identified genes associated with parkinsonism include the oncogene DJ-1, the MAPT (tau) gene, progranulin (PGRN), and PINK1 [23-29].

Neuroanatomic abnormality

According to different studies Parkinson's disease (PD) does not only affect the brain or the central nervous system, but the entire body. In fact, it is widely believed that the disease starts in the peripheral nervous system, in areas such as the intestine, where the nature and features of the disease can be present many years before involving the brain. The autonomic nervous system, which controls many automatic functions such as breathing and movements of the intestines, is affected, leading to characteristic signs and symptoms ranging from constipation to pain to skin changes. While the brain involvement is responsible for the core features, other affected locations contribute to the complicated picture of PD [9,23].

The most common symptoms of PD result from the loss of neurons in a part of the brain called the substania nigra. The affected brain cells of people with PD contain Lewy bodies—deposits of the protein alpha-synuclein. Researchers do not yet know why Lewy bodies form or what role they play in the disease. Some research suggests that the cell's protein disposal system may fail in people with PD, causing proteins to build up to harmful levels and trigger cell death. Additional studies have found evidence that clumps of protein that develop inside brain cells of people with PD may contribute to the death of neurons. Some researchers speculate that the protein buildup in Lewy bodies is part of an unsuccessful attempt to protect the cell from the toxicity of smaller aggregates, or collections, of synuclein [24,25].

Researchers identified that in Parkinson's disease (PD) there is mild frontal atrophy with loss of the normal dark melanin pigment of the midbrain. Microscopically there is degeneration of the dopaminergic cells with the presence of Lewybodies (LBs) in the remaining neurons and processes of the substantia nigra pars compacta (SNpc); other brainstem nuclei; and regions such as the medial temporal, limbic, and frontal cortices. LBs have a high concentration of α-synuclein and are the pathologic hallmark of the disorder. Mutations in the α-synuclein gene can cause familial PD by promoting the formation of α-synuclein-positive filaments that aggregate into LBs and Lewy neurites It is now generally accepted that this pathology appears first in the anterior olfactory nuclei and lower brainstem (glossopharyngeal and vagal nerve nuclei), with ascending brainstem involvement of the locus coeruleus n. giganto cellularis, and the raphe, before extending to the magnocellular nuclei of the basal forebrain, the central nucleus of the amygdala, and the SNpc. Further progression extends to the thalamus and cerebral cortex. Involvement of these extra nigral areas is postulated to play a role in the non-motor (e.g., autonomic, sleep, emotional, and cognitive) and levodopa unresponsive motor aspects (e.g., postural instability, gait, and bulbar disturbances) of PD [23,26].

According to different studies in patients with Parkinson's disease the presence of five adjacent but anatomically distinct fronto-cortico-striato-thalamic loops with motor, oculomotor, limbic, anterior cingulate, and prefrontal targets and that dysfunction of these neural loops is linked to the motor and non-motor features in Parkinson's disease and other basal ganglia disorders. A common feature of these cortical–subcortical loops is their projection from higher-level cortical areas to the basal ganglia via striatal areas with outflow through the internal globus pallidum (Gpi) or its histological analog, the substantia nigra pars reticulata (SNpr). Gpi/SNpr outputs then project to specific areas of the thalamus that complete the loops through projections to the original cortical area. Within each loop, the striatonigral component includes a "direct" pathway that projects directly from striatum to Gpi/SNpr and an "indirect" pathway that flows from the striatum through the subthalamic nucleus (STN) to reach the Gpi/SNpr [23-26].

Neurotransmitters (Biochemical factors)

In Parkinson's disease the most common symptoms result from the loss of neurons in an area near the base of the brain called the substantia nigra. Normally, the neurons in this area produce an important brain chemical known as dopamine. Dopamine is a chemical messenger responsible for transmitting signals between the substantia nigra and the next "relay station" of the brain, the corpus striatum, to produce smooth, purposeful movement. Loss of dopamine results in abnormal nerve firing patterns within the brain that cause impaired movement. Studies have shown that most people with Parkinson's have lost 60 to 80 percent or more of the dopamine-producing cells in the substantia nigra by the time symptoms appear. The primary pathology in Parkinson's disease is loss of dopaminergic neurons in the ventral tier of the substantia nigra pars compacta (SNpc), but what leads to this selective and progressive cell death is unknown [31-34].

The biochemical consequence of dopaminergic cell loss in the SNpcis gradual denervation of the striatum, the main target projection for the SNpc neurons. Other target regions of these neurons include the intralaminar and parafascicular nuclei of the thalamus, the globus pallidus, and the subthalamic nucleus (STN). Dopamine denervation of theputamen, the motor portion of the striatum, leads to many of the motorsymptoms of PD. Symptoms develop when striatal dopamine depletionreaches 50–70% of normal. Pharmacologic restoration of dopaminetransmission is the basis for symptomatic drug treatment of PD [33,34].

Environmental factors

Exposure to certain toxins has caused parkinsonian symptoms in rare circumstances (such as exposure to MPTP, an illicit drug, or in miners exposed to the metal manganese). Other still unidentified environmental factors may also cause PD in genetically susceptible individuals [19-22].

Epidemiology

Global prevalence of Parkinson's disease

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease, and it affects over 1 percent of the population over age 55 and nearly 3 percent of the population over age 70. The mean age of onset for Parkinson's disease is 60 years of age, and 80 percent of individuals develop the disorder between the ages of 40 and 70 years. About 5 percent of patients have symptom onset

before age 40, and, in such cases, the disease is classified as young onset Parkinson's disease. Juvenile onset occurs in less than 1 percent of cases. The wide range in the age of onset of Parkinson's disease contributes to misdiagnosis, especially in younger patients [35-37].

Socio demographic factors

PD affects about 50 percent more men than women, and the reasons for this discrepancy are unclear. While PD occurs in people throughout the world, a number of studies have found a higher incidence in developed countries. Other studies have found an increased risk in people who live in rural areas with increased pesticide use. However, those apparent risks are not fully characterized. One clear risk factor for PD is age. The average age of onset is 60 years, and the incidence rises significantly with advancing age [7,8,36].

Young onset and juvenile parkinsonism

One clear risk factor for PD is age. The average age of onset is 60 years, and the incidence rises significantly with advancing age. However, about 5 to 10 percent of people with PD have “early-onset” disease that begins before the age of 50. Some early onset cases are linked to specific gene mutations such as parkin. People with one or more close relatives who have PD have an increased risk of developing the disease themselves, but the total risk is still about 2 to 5 percent unless the family has a known gene mutation for the disease. An estimated 15 to 25 percent of people with PD have a known relative with the disease. In very rare cases, parkinsonian symptoms may appear in people before the age of 20. This condition is called juvenile parkinsonism. It often begins with dystonia and bradykinesia, and the symptoms often improve with levodopa medication [38-40].

Early onset Parkinson's disease (EOPD) is Parkinson's disease (PD) with onset at < 41 years of age. Within EOPD, there appear to be two groups namely: young onset Parkinson's disease (YOPD), with onset between 21 and 40 years, and juvenile parkinsonism (JP), with onset at < 20 years. The two major clinical differences between these groups are a higher familial occurrence of PD and dystonia in juvenile parkinsonism (JP) [38-40].

Diagnosing Parkinson's Disease

The diagnosis of Parkinson's disease is clinically based because there is no biological marker for the disease. A diagnosis of Parkinson's disease (PD) can be made with some confidence in patients who present with at least two of the three cardinal signs-rest tremor, rigidity, and bradykinesia. Tremor is particularly important, as it is present in 85% of patients with true PD; a diagnosis of PD is particularly difficult when tremor is absent. The initial symptoms in up to 20 percent of patients are non-motor, including fatigue, musculoskeletal complaints, and depression. Other non-motor somatic symptoms of Parkinson's disease include sialorrhea, dysarthria, visual and genitourinary dysfunction, sleep disturbances, sweating, seborrhea, edema, constipation, paresthesias, and a decreased sense of smell. In many patients, there is clear evidence for a prodromal phase, lasting about 4 to 8 years before the onset of obvious motor signs and often characterized by depression, anxiety, and musculoskeletal discomfort. A unilateral and gradual onset of symptoms further supports the diagnosis. Masked facies, decreased eye blinking, stooped posture, and decreased arm swing complete the early picture. The onset may also be heralded by vague feelings of weakness, fatigue, aching, and discomfort. The initial symptoms in up to 20 percent of patients are non-motor, including fatigue, musculoskeletal complaints, and depression. Other non-motor somatic symptoms of Parkinson's disease include sialorrhea, dysarthria, visual and genitourinary dysfunction, sleep disturbances, sweating, seborrhea, edema, constipation, paresthesias, and a decreased sense of smell [41,42].

Comorbid Mental Disorders with Parkinson's Disease

Psychiatric disturbances affect up to 90 percent of patients at some point during the course of Parkinson's disease, and more than one psychiatric disturbance is often present. Early in the disease process, adult-onset anxiety and depressive disorders precede the obvious onset of motor symptoms in up to 30 percent of patients [37,41,43-45].

Depression

Normal psychological reactions to the illness can result in low mood, grief, demoralization, frustration, and embarrassment. Depression in Parkinson's disease (PD) is common, and its impact can equal that of the motor symptoms. Depressive disorders in Parkinson's disease involve more pervasive mood changes and generally resemble idiopathic forms of depression. In non-depressed patients with Parkinson's disease, motor symptoms can limit the ability to pursue previous interests, such as detailed woodworking, but patients with depressive disturbances will fail to find alternative activities to enjoy that are within their physical capacities. prevalence rates range from 20 to 90 percent, with an average reported frequency of 40 to 50 percent. Up to half of those with depression, in most studies, have major depression [41,43]. It is often difficult to diagnose due to the overlap between the somatic and vegetative symptoms of PD and depression. As a result, depression may go unrecognized and untreated. There is compelling evidence that depression in PD is an intrinsic part of the illness and not simply a reaction to disability. Recognizing even mild depression is particularly important since it can account for otherwise unexplained albeit reversible worsening of parkinsonian motor symptoms, new somatic symptoms, and sleep disruption. Depression can also be induced or aggravated iatrogenically by anti-parkinsonian and psychotropic agents used to treat other symptoms. Other psychological, vegetative, and autonomic features of depression are also common, but early morning awakening, anergia, and retardation occur at comparable rates in non-depressed Parkinson's disease patients. Depression is generally not associated with a family history of mood disorders [41,43].

Anxiety

Anxiety is common in patients with Parkinson's disease and can interfere with their response to treatment. Anxiety disorders in PD can appear in isolation or as an accompaniment of depression or progressive cognitive impairment. Anxiety disorders, particularly generalized anxiety, panic, and social phobia, occur in up to 40% of patients with Parkinson's disease (PD). They can also be due to an akathisia equivalent provoked in part by under treatment of motor symptoms. The development of drug-induced motor fluctuations can compound the problem by precipitating anxiety during the off periods that, in severe cases, may mimic panic attacks. Particularly common are generalized anxiety disorder, social phobia, and panic disorder, which has a prevalence rate of 25 percent in some series. In general, the anxiety syndromes in Parkinson's disease resemble those in idiopathic conditions and frequently co-occur with depression [41].

Cognitive impairment

Some degree of cognitive impairment, ranging from mild executive dysfunction to dementia, affects nearly all patients with Parkinson's disease; about 25 to 40 percent of patients develop dementia. These occur in the later stages of the illness and present as frontal lobe dysfunction. Difficulties with complex tasks, long-term planning, and memorizing or retrieving new information are common. Although some of these symptoms represent bradyphrenia (the cognitive equivalent of bradykinesia), it is now clear that the dysfunction also includes working memory, executive function, attention, mental flexibility, visuospatial function, and word fluency. In contrast, language and simple mathematical skills are relatively spared, unlike in patients with AD. Iatrogenic contributors to cognitive decline in vulnerable patients include the use of anticholinergics, amantadine, psychotropics, and even dopaminomimetic medications. Depression and intercurrent medical illnesses, especially infections (of the urinary tract or elsewhere) and dehydration, are important reversible causes of an acute change in cognitive function in PD [37].

The incidence of significant dementia in PD may be as high as six times that in age-matched controls and, in subspecialty clinics, can be as high as 70% or greater with long-term observation. In late stages the presence of substantial cognitive impairment may limit therapeutic options and contribute more to overall disability than the motor symptoms in PD [37].

Psychosis

Psychosis affects about 20 percent of patients, Parkinson's disease who receive long-term treatment with dopaminergic agents (e.g., levodopa, bromocriptine, pergolide ropinerole, and pramipexole) identified by the presence of chronic hallucinations and delusions, with up to 50 percent of patients experiencing hallucinations over the course of their illness. Psychosis most commonly occurs in patients who have associated cognitive impairment. Clinically this presents as a delirium-a confusional psychosis [44,45].

Apathy

Apathy is a valid behavioural syndrome in Parkinson's disease and is associated with depression and cognitive deficits. Apathy occurs in at least 25 percent of patients and often coexists with depression. It is manifest as indifference and a lack of motivation, initiative, perseverance, interest in new things, or concern for one's health [41].

Management of Parkinson's Disease

There's currently no cure for Parkinson's disease, but treatments are available to help relieve the symptoms and maintain your quality of life. Although dopamine agonist medications are the mainstay of the treatment for Parkinson's disease, research has found that Surgery, psychosocial interventions, including psychotherapy diet and physical exercise, can augment the clinical improvement. Just as pharmacological agents are used to treat presumed chemical imbalances, no pharmacological strategies must treat any biological issues. The complexity of Parkinson's disease usually renders any single therapeutic approach inadequate to deal with the multifaceted disorder. Psychosocial modalities should be integrated into the drug treatment regimen and should support it. Patients with Parkinson's disease benefit more from the combined use of drugs and psychosocial treatment than from either treatment used alone [10-18].

The goals of therapy in PD are to maintain function and quality of life and to avoid drug-induced complications. Bradykinesia, tremor, rigidity, and abnormal posture respond well to symptomatic therapy early in the course of the illness. In contrast, cognitive symptoms, hypophonia, autonomic dysfunction, and imbalance tend to respond poorly. Primary motor disability in PD is often aggravated by secondary disability resulting from physical deconditioning following a sedentary lifestyle. Prevention of secondary disability requires a consistent program of physical exercise. Multiple open-label studies of exercise in PD support the importance of regular activity [16-18].

Pharmacological management

Current treatment options for Parkinson's disease provide only symptomatic relief of the motor deficits as there are no known preventatives or regenerative strategies. Medications for Parkinson's disease (PD) fall in to three categories. The first category includes drugs that increase the level of dopamine in the brain. The most common drugs for PD are dopamine precursor substances such as levodopa that cross the blood-brain barrier and are then changed into dopamine. Other drugs mimic dopamine or prevent or slow its breakdown. The second category of PD drugs affects other neurotransmitters in the body in order to ease some of the symptoms of the disease. For example, anticholinergic drugs interfere with production or uptake of the neurotransmitter acetylcholine. These can be effective in reducing tremors. The third category of drugs prescribed for PD includes medications that help control the non-motor symptoms of the disease, that is, the symptoms that don't affect movement. For example, people with PD-related depression may be prescribed antidepressants.

The gold standard of treatment for Parkinson's disease is levodopa, which increases the life expectancy among Parkinson's disease patients and significantly improves function and quality of life. Nerve cells can use levodopa to make dopamine and replenish the brain's reduced supply. People cannot simply take dopamine pills because dopamine does not easily pass through the blood-brain barrier. Usually, people are given levodopa combined with another substance called carbidopa. When added to levodopa, carbidopa prevents the conversion of levodopa into dopamine except for in the brain; this stops or diminishes the side effects due to dopamine in the bloodstream. Levodopa/carbidopa is often very successful at reducing or eliminating the tremors and other motor symptoms of PD during the early stages of the disease. It allows the majority of people with PD to extend the period of time in which they can lead active, productive lives. Although levodopa/carbidopa helps most people with PD, not all symptoms respond equally to the drug. Levodopa usually helps most with bradykinesia and rigidity. Problems with balance may not respond [10-16].

During early stages, anticholinergic medications such as trihexyphenidyl (Artane) or benztropine (Coglutin), amantadine (Symmetrel), and the monoamine oxidase inhibitors (MAOIs), selegiline (Eldepryl) and rasagaline (Azilect), provide mild to moderate reductions in motor symptoms. Dopamine agonists such as pramipexole (Mirapex), ropinirole (Requip), and rotigotine (Neupro) and/or levodopa may then be added to address progressive disability. Pergolide (Permax), a dopamine agonist used for many years in patients with Parkinson's disease, was recently found to be associated with cardiac valve damage and is no longer available for use. Dopamine agonists are especially effective early treatments that can

delay initiation of levodopa therapy. Postural instability does not usually respond to antiparkinsonian medications [10-16].

Surgery

Before the discovery of levodopa, surgery was standard treatments for tremor and rigidity in Parkinson's disease. Studies in the past few decades have led to great improvements in surgical techniques, and surgery is again considered for people with PD for whom drug therapy is no longer sufficient. More refined stereotactic neurosurgical therapies currently used for Parkinson's disease involve high-frequency deep brain stimulation (DBS) of the STN and Gpi or ablative procedures that target the GPi (pallidotomy) or thalamus (thalamotomy). Both improve motor function because they reduce the hyperactivity of the STN and its efferent targets, thus partially restoring thalamic outflow. Thalamotomy and thalamic DBS are indicated for disabling tremor. Because these procedures cause permanent destruction of small amounts of brain tissue, they have largely been replaced by deep brain stimulation for treatment of PD. However, a new method using focused ultrasound from outside the head is being tested because it creates lesions without the need for surgery [46].

Complementary and Supportive Therapies

There are several therapies that can make living with Parkinson's disease easier and help you deal with symptoms on a day-to-day basis. A wide variety of complementary and supportive therapies may be used for PD. Among these therapies are standard physical, occupational, and speech therapy techniques, which can help with such problems as gait and voice disorders, tremors and rigidity, and cognitive decline. Other types of supportive therapies include [17-19].

Physiotherapy

Exercise programs are recommended in people with Parkinson's disease. There is some evidence that speech or mobility problems can improve with rehabilitation, although studies are scarce and of low quality. A physiotherapist can work to relieve muscle stiffness and joint pain through movement (manipulation) and exercise. The physiotherapist aims to make moving easier, and improve walking and flexibility. They also try to improve fitness levels and ability to manage things for you. Regular physical exercise with or without physiotherapy can be beneficial to maintain and improve mobility, flexibility, strength, gait speed, and quality of life. When an exercise program is performed under the supervision of a physiotherapist, there are more improvements in motor symptoms, mental and emotional functions, daily living activities, and quality of life compared to a self-supervised exercise program at home [47,48]. Exercise can help people with PD improve their mobility and flexibility. The effects of exercise on disease progression are not known, but it may improve body strength so that the person is less disabled. Exercises also improve balance, helping people minimize gait problems, and can strengthen certain muscles so that people can speak and swallow better. Exercise can improve emotional well-being and general physical activity, such as walking, gardening, swimming, calisthenics, and using exercise machines, can have other benefit. An NINDS-funded clinical trial demonstrated the benefit of tai chi exercise compared to resistance or stretching exercises [16,17,47,48].

Many people with Parkinson's disease have swallowing difficulties (dysphagia) and problems with their speech. A speech and language therapist can often help you improve these problems by teaching speaking and swallowing exercises, or by providing assistive technology. Speech therapy and specifically LSVT may improve speech. Occupational therapy (OT) aims to promote health and quality of life by helping people with the disease to participate in as many of their daily living activities as possible. There have been few studies on the effectiveness of OT and their quality is poor, although there is some indication that it may improve motor skills and quality of life for the duration of the therapy [49-51].

Diet therapy

For some people with Parkinson's disease, making dietary changes can help improve some symptoms. These changes can include: increasing the amount of fibre in the diet and drinking enough fluid to reduce constipation, increasing the amount of salt in your diet and eating small, frequent meals to avoid problems with low blood pressure, such as dizziness. While there is currently no proof that any specific dietary factor is beneficial, a normal, healthy diet can promote overall well-being for people with PD just as it would for anyone else. Eating a fiber-rich diet and drinking plenty of fluids also can help alleviate constipation. A high protein diet, however, may limit levodopa's absorption, highlighting the importance of the timing of medications.

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