

## Parkinson's Disease: Promising Strategies to Tame Symptoms

Every day, researchers around the world are working on new ways to improve the lives of the 4 to 6 million people estimated to be living with Parkinson's disease—the degenerative movement disorder that leads to trembling, stiffness and difficulty walking and speaking as it progresses. Although no cure for Parkinson's exists, a number of therapies offer relief from the disease's troublesome symptoms and improve quality of life. If you or a loved one is living with Parkinson's disease, here's what you should know about ongoing research—and which strategies potentially offer the greatest benefit.

### Exercise: A top priority

Several new studies have suggested that various forms of exercise, including tai chi and weight lifting, may reduce some physical symptoms associated with Parkinson's. Examining exercise's effects on Parkinson's is a hot area of research—and with good reason. Physical activity has been shown to help slow the deterioration of motor functions and prolong independence.

Some researchers believe that exercise could emerge as an intervention that may ultimately slow the progression of Parkinson's by protecting the brain. The disease results in the loss of dopamine-producing brain cells. Exercise improves blood circulation and oxygen flow to the brain, which may prove to slow brain-cell death.

Other experts believe that well-conditioned bodies may be better able to stave off some early symptoms, though brain-cell death may still be progressing at the same rate as without exercise.

Although medications are quite effective at controlling some Parkinson's motor symptoms such as slowing and stiffness, other symptoms such as balance problems are less responsive to drugs but may respond to exercise. For example, a study

of nearly 200 people with mild-to-moderate Parkinson's disease found that practicing tai chi, a gentle, balance-based exercise, appeared to reduce balance problems and falls associated with the disease.

Researchers found that people who participated in 60-minute tai chi sessions twice weekly for 24 weeks saw marked improvements in balance control when compared with people who participated instead in stretching or training with resistance bands. The benefits persisted for at least three months after the study.

Tai chi may reduce dyskinesia, or involuntary movements, associated with Parkinson's by helping people develop effective sway strategies to better control balance, according to the study, published in the February 9 issue of the *New England Journal of Medicine*. This effect can translate to improvement in performing everyday activities such as walking, removing items from a cabinet and standing up.

Weight lifting may also ease Parkinson's symptoms, according to a small government-funded study at the University of Illinois at Chicago. Among a group of 48 Parkinson's patients, those who lifted weights twice a week saw more improvement with tremors between 12 and 24 months after starting a weight-lifting program than people who did a mix of stretching, balance, strengthening and aerobic exercises during that same period.

After 24 months, those in the weight-lifting group saw a significant reduction in tremors. In fact, weight lifting resulted in a similar reduction in symptoms as seen with the powerful Parkinson's drug levodopa. The results were presented at the annual American Academy of Neurology meeting last April.

### A reduction in 'off' times

Even though oral medications like levodopa can markedly reduce Parkinson's motor symptoms, patients with advanced disease still experience "off" times—the disruptive effects of tremor, slowness and stiffness at times late in the day when the beneficial effects of drugs begin to wear off before the

### Slowing disease progression

Scientists are not only investigating how to better treat Parkinson's symptoms, but also how to slow its progression. Several promising clinical trials are currently being conducted. The National Institutes of Health is involved in the largest-ever series of Parkinson's clinical trials with more than 1,700 patients enrolled. The ongoing five-year study, called Neuroprotection Exploratory Trials in Parkinson's Disease (NET-PD), is testing several drug therapies for their neuroprotective effect (the ability to delay disease progression).

The ADAGIO trial investigated the MAO-B inhibitor agent rasagiline, which helps block the breakdown of dopamine, to see whether it has the ability to slow the progression of Parkinson's. The trial results were inconclusive but promising: There's some indication that rasagiline may be able to delay disease progression, but further study is needed. Doctors currently use MAO-B inhibitors to reduce Parkinson's symptoms.

Another major area of research focuses on identifying Parkinson's biomarkers. The Michael J. Fox Foundation's Parkinson Progression Markers Initiative (PPMI) is considered by many to be the most important clinical research effort globally at the moment. The five-year study's goal is to identify progression biomarkers—biological characteristics that can track Parkinson's progression and reveal how severe a patient's disease is. Such biomarkers will enable researchers to design more effective clinical trials to develop new and better treatments as well as diagnose the disease before symptoms appear.

### Long-term improvements with deep brain stimulation

Deep brain stimulation (DBS) surgery is an accepted treatment for the neurological symptoms of Parkinson's disease. DBS is most helpful to Parkinson's patients suffering from motor fluctuations and dyskinesias, or involuntary movements. DBS is also being used or tested in movement disorders other than Parkinson's as well as in a variety of neurological and behavioral disorders.

During DBS, surgeons implant a thin wire electrode in the brain and connect it to a small, battery-operated device called an implantable pulse generator (IPG), which is placed under the collarbone. The device is similar to a heart pacemaker. The IPG delivers electrical signals through the electrode to areas of the brain that control movement, blocking the abnormal nerve signals that trigger tremor and other Parkinson's symptoms.

next pill is scheduled to be taken.

Doctors address this temporary "wearing off" time in several ways, such as increasing the drug's dose or shortening the dose intervals. Now researchers have developed a levodopa-carbidopa intestinal gel (LCIG) that may work better than the standard oral medication at reducing off time in patients with advanced Parkinson's and helps with highly disabling motor fluctuations that are extremely difficult to manage with oral drugs alone. An external portable pump infuses the intestinal gel through a tube implanted in the intestine, similar to a feeding tube.

Researchers found that LCIG reduced off time by an average of nearly two extra hours a day compared with the oral drug combination during 16 hours a day of continuous pump use. At the study's start, the average participant experienced about 6.6 hours a day of off time.

Researchers from Mount Sinai School of Medicine in New York presented the results of the trial, supported by Abbott Laboratories, the gel's maker, at the American Academy of Neurology meeting last April. More investigational study is being done in the United States; however, LCIG is already approved for use in 40 other countries, according to Abbott.

### Benefits of caffeine

Parkinson's disease can cause excessive daytime sleepiness in some people. Since caffeine is commonly used to increase daytime alertness in the general population,

researchers have begun to look at its use as a potential Parkinson's treatment.

Past studies have linked lifelong caffeine use with a lower risk of developing Parkinson's disease, and studies of animals suggest that caffeine may improve motor function in Parkinson's patients. But few studies have examined its effects on Parkinson's symptoms in humans.

A randomized, controlled trial of 61 patients in Canada found that those given 100 to 200 milligrams of caffeine (about the equivalent of one to two cups of coffee) twice daily for six weeks had no significant reduction in daytime sleepiness over those receiving a placebo. However, the study found that the patients receiving caffeine saw a slight improvement in their motor function. The results, published online in August in *Neurology*, suggest that this potential benefit needs to be further studied in longer and larger trials.

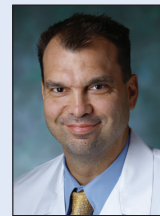
### A 'sleep benefit'

Scientists in the Netherlands recently investigated the intriguing phenomenon reported by some Parkinson's patients known as "sleep benefit"—improved motor functioning upon waking in the morning. Sleep benefit seems contrary to what would be expected after a night without medication. The researchers found that nearly half of patients they studied reported experiencing sleep benefit in the morning, while roughly one-third reported improved motor function following an afternoon nap. It's unclear what causes sleep benefit

or why some Parkinson's disease patients experience it but others don't.

Another small study published in August in the journal *Brain* reported that sleep might also give people with Parkinson's a memory boost. Some patients have problems remembering information and applying it to tasks, but a good night's sleep helped study participants perform better on a memory test the next morning—a marked improvement over patients who didn't get sufficient sleep, often because of a sleep disorder like sleep apnea. This finding prompted the study authors to recommend that doctors test and treat Parkinson's patients for sleep disorders.

### DOCTOR'S VIEWPOINT



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**Getting exercise** should be a top priority for people who have Parkinson's disease. But activity can be daunting: The ability to perform and control simple movements, let alone exercises, is difficult. Tai chi is a good option

for many patients because of its slow, deliberate movements and its ability to improve balance and gait. Even a little exercise can help.

Drugs can be effective in reducing tremors, but some people can't tolerate their side effects. Deep brain stimulation (DBS) won't offer a greater benefit than medication, but it may help reduce some of the debilitating drug side effects. It's also a common misconception that DBS is a last-ditch treatment option for patients who can no longer manage symptoms with drugs. In fact, selecting the right patient is critical for the success of DBS. Generally, good candidates for DBS are those who still respond to medication but are experiencing severe motor fluctuations associated with levodopa.