

Parkinson disease and mortality

Understanding how the two are connected

Steven Karceski, MD

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Parkinson disease (PD) is the second most common neurodegenerative neurologic illness, after Alzheimer disease (AD). In both illnesses there is a gradual loss or decrease in the number of nerve cells, called neurons. Although similar in this regard, the 2 illnesses are very different: AD primarily causes troubles with thinking and memory while PD mostly causes problems with movement. However, some people with PD also experience troubles with thinking, called mild cognitive impairment (MCI). When the two occur together, this is referred to as PD-MCI. In addition, there are many studies that have shown that people with PD have a shorter lifespan than people without PD. In their study “Early predictors of mortality in parkinsonism and Parkinson disease: a population-based study,” Dr. Backstrom and his colleagues looked at many factors to better understand the link between PD and earlier mortality.

How did they do this?

Dr. Backstrom works at Umea University, in Sweden. He and his colleagues work in an area in northern Sweden where approximately 142,000 people live. Umea University is the main medical center in this region, and most (if not all) of the people who live there are referred to Umea University. In order to better understand the connection between PD and early death, Dr. Backstrom enrolled only people who had early PD and who were not yet taking medication for this. People were enrolled between January 1, 2004, and April 30, 2009, and were followed until August 31, 2017. Dr. Backstrom identified 182 people with symptoms of early PD.

In the study, many tests were done (table). All of the participants had neurologic examinations, filled out questionnaires, and had neuropsychological testing. Not everybody had the other tests (table). The first test was a detailed neurologic examination in order to confirm and firmly establish the diagnosis of PD. This is essential because there are several illnesses that are very similar to PD, and Dr. Backstrom wanted to be sure that the diagnosis was as precise as possible. Of the 182 patients, Dr. Backstrom found that 143 had classic (also called idiopathic) PD, 13 had a similar disease called multiple system atrophy (MSA), and 18 had progressive supranuclear palsy (PSP). The other 8 had an unclear diagnosis or simply did not have PD.

The study was designed to look at the association of mortality with PD. During the study, 109 people died. For 98 of these (90% of the people who died), a cause of death was known.

What did the study show?

During up to 13.5 years of follow-up, Dr. Backstrom first looked at mortality, and how this was associated with the underlying diagnosis. One thing the researchers noted was that the most common cause of death was pneumonia. A total of 53.8% of the people with PD died during the study. This was in comparison to 92.3% of those who were found to have the more serious PSP or 88.9% of those who had MSA.

The patients with PD were broken down into 2 groups: those who had MCI (PD-MCI) and those who did not (PD only). For those who had PD without cognitive impairment, the death rate was no different from that of the general Swedish population. However, for those who had PD-MCI, the risk of dying was 2.4 times higher. Another way of thinking about this is as follows: if you started the study when you were 71, you would be expected to survive 11.6 years, which

Table Tests performed

Test	No. of patients who had the test	What is the test?	Why was it done?
Neurologic examination	All	Complete neurologic evaluation	Confirm diagnosis of PD
Postural imbalance and gait disorder	All	A specific measure of items evaluated in people with PD	Identify people who have these symptoms
Parkinson Disease Questionnaire (39 questions)	All	Questionnaire	Confirm diagnosis of PD
Mini-Mental State Examination	All	A quick assessment of a person's thinking	Identify people who may be experiencing memory problems or difficulties in their thinking
Montgomery-Åsberg Depression Rating Scale	All	Mood	Determine if a person also had depression
CSF analysis (lumbar tap)	120	White blood cell count	A measure of inflammation
		Tau	An abnormal protein
		AB1-42	An abnormal protein
		α-Synuclein	An abnormal protein
DaT scan	170	Nuclear medicine study	Identifies areas of reduced brain function
Genetic testing	135	A specific gene (<i>APOE</i>)	A gene that has been associated with Alzheimer disease
Neuropsychological testing	All	A battery of tests for memory and cognition	To assess and reassess a person's thinking—this test was done at the beginning, and was repeated after 1 year, 3 years, 5 years, and 8 years

Abbreviation: PD = Parkinson disease.

was the same as Swedish people without PD. If you had PD-MCI, survival was 8.2 years, about 3 years less than would otherwise be expected.

When looking at all of the tests, Dr. Backstrom found that mortality was increased if a person had 1 or more of the following: PD-MCI, postural imbalance and gait disorder, reduced uptake in certain brain regions on the DaT scan, and an elevated white blood cell count in the CSF analysis.

What does this mean?

Do all people with PD die younger? Or are there more specific reasons why this happens? Many studies have shown that people with PD die at an earlier age than otherwise healthy adults. However, it has been unclear in many of these studies if there are specific factors that lead to early death. Dr. Backstrom's study is important for many reasons. First, it showed that when a person has PD without cognitive problems, life expectancy is the same as in the general population. If a person had an atypical type of PD (like MSA or PSP), life expectancy was reduced. Similarly, those who had both PD and cognitive problems had a shorter life span than the general population.

During the study, 120 of the 182 people agreed to have a lumbar puncture (also known as a spinal tap). This is not

a usual test to evaluate people with PD. However, in 13.1%, the CSF showed a high white blood cell count. In this group, the risk of death was 6.31 times higher. It is difficult to know what this means, given the small number. Further study is needed.

What is PD?

PD is named after James Parkinson. He first described the illness in 1817. PD primarily causes problems with movement. PD causes a person to move very slowly: this is called bradykinesia. A person with PD appears stiff or rigid. Patients often develop a slightly stooped posture, and will begin to have a very characteristic pattern to their walking. They may shuffle their feet, and take very small, frequent steps (called festination). At times, a person with PD may appear to suddenly freeze up or be unable to move for a short period of time. When a person has PD, he or she often will have 1 or more of these symptoms.

A tremor of the hands is common. In fact, tremor is the most characteristic physical finding in PD. The tremor is called a pill-rolling tremor. It gets its name because of how the tremor appears. Years ago, pharmacists used to make their own tablets. In order to make medications into a pill, they would roll the medicine into a small, round ball. In order to

roll a small ball, the hand has to move in a very specific way. This hand movement looks very similar to the tremor in PD.

What causes PD?

In PD, the underlying problem has to do with a neurotransmitter called dopamine. A small number of specific brain cells make dopamine. These brain cells are located in an area of the brain called the substantia nigra. The substantia nigra is in a deep part of the brain called the brainstem. Though only a few cells make dopamine, these cells send the neurotransmitter to many different regions of the brain. Changes in dopamine levels therefore can have widespread effects within the brain.

When we are young, our brains make plenty of dopamine. As we get older, this amount decreases. In PD, the amount of dopamine becomes critically low. In PD, these changes occur very slowly: the amount of dopamine gradually decreases over time. The gradual loss of dopamine causes the gradual worsening of movement. This is why, in early PD, the symptoms may be very subtle or mild.

Treatment of PD

Understanding the link between dopamine and PD was critical to the development of many treatments. The answer seems simple enough: take dopamine. However, the body does not allow dopamine to cross over into the brain, where it is needed. This is why people with PD take a medication called levodopa. Levodopa can cross over into the brain. The brain converts the medication into dopamine.

Saying this, there are many other treatments for PD. For the most part, these treatments are aimed at increasing the amount

of dopamine in the brain. Some treatments help to keep the dopamine where it is needed most. Other treatments, like deep brain stimulation, are aimed at the system of brain cells that function together to create smooth, graceful movements. Electrical impulses, when applied to this delicate network of brain cells, reduces tremor and improves a person's mobility.

Every person is different. A physician may not know which treatment is best for a specific person. This is because there is no optimal blood test or scan that would help a doctor to know which treatment option (or options) will work the best. Studies are limited: they can tell us which medicines/treatments are effective, but they do not tell us which ones work best for a specific person. A person with PD can become frustrated if the first treatment does not work. To make things even more complicated, some people may need a combination of treatments in order to feel well. In these instances, several treatments may need to be tried before the best treatment plan can be found. By talking honestly with your doctor, the best treatment or combination of treatments can be found.

For more information

Brain & Life

brainandlife.org

American Parkinson Disease Association

apdaparkinson.org/

Michael J. Fox Foundation for Parkinson's Research

michaeljfox.org

Parkinson Alliance

parkinsonalliance.org/

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