NIEHS
National Institute of Environmental Health Sciences

Parkinson's and the Environment: Unraveling the Links

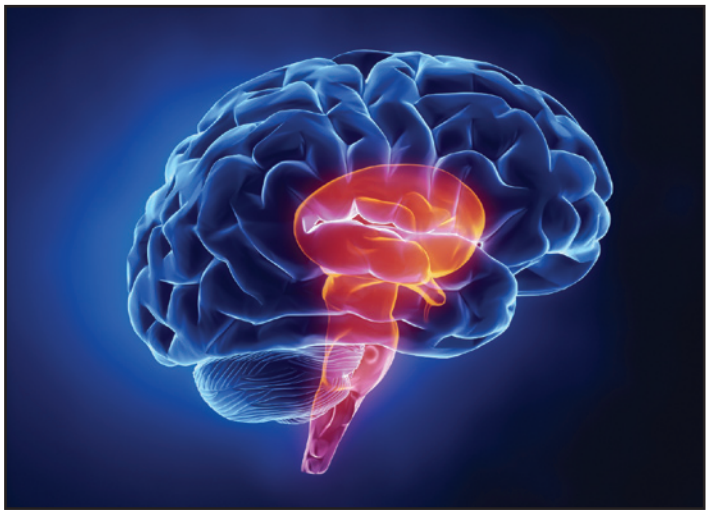
Glenn Smith, 64, stepped off a curb one day, felt a ping in his foot, and began experiencing pain. His walking gait changed, and his right arm didn't swing as usual and felt heavy.

The symptoms, however, remained a mystery, until Glenn read a magazine article about actor Michael J. Fox and said to himself, "I wonder if I have Parkinson's disease." A neurologist confirmed that he did.

Glenn, an executive with a company that manages trade associations, continued his life as usual. But symptoms worsened. He felt severe fatigue. His handwriting became illegible. His voice grew softer and softer until it was difficult to hear him on the telephone. He had to stop driving after finding himself drifting off the road. His wife has taken over paying bills, since some were falling through the cracks, and he retired earlier than planned.

Defining Parkinson's

Parkinson's disease is a chronic neurodegenerative disease, the second most common disorder of this type after Alzheimer's disease. It progresses slowly as small clusters of cells in the midbrain die.



The gradual loss of these cells results in reduction of a critical neurotransmitter called dopamine, the chemical responsible for transmitting messages to the parts of the brain that coordinate muscle movement.

Genetics is not considered the major contributing factor for Parkinson's disease. However, NIEHS-funded researchers have identified many gene variations that make people more susceptible to environmental toxins that may trigger the development of Parkinson's disease. In the 5 to 10 percent of cases in which symptoms begin before the age of 50, genetics seems to play a bigger role.

A National Problem

Currently, about a million Americans suffer from Parkinson's disease, with about 60,000 new cases diagnosed each year. The average age of onset is about 60. The aging of America — members of the baby boomer generation began turning 65 in January 2012 — has major implications for both individual suffering and national health care costs.

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NIH...Turning Discovery Into Health

According to the Parkinson's Disease Foundation, the combined direct and indirect costs of Parkinson's, including treatment, social security payments, and lost income from inability to work, are estimated to be nearly $25 billion per year in the United States alone.[1]

Parkinson's disease strikes people of all races, ethnic groups, nationalities, and income levels. Former U.S. Attorney General Janet Reno and boxer Muhammad Ali, in addition to Fox, are among the famous people living with Parkinson's disease.

Attacking Parkinson's

Research funded by NIEHS, one of a number of NIH institutes involved in studying different aspects of Parkinson's disease, focuses on environmental factors. While prevention is the most obvious benefit from such research, findings are also unraveling clues about how to diagnose the disease, to treat it by controlling symptoms, and to slow or even stop progression.

NIEHS has created three Centers for Neurodegeneration Science at UCLA, Emory University, and The Parkinson's Institute and Clinical Center. Additionally, NIEHS arranges workshops and panels where researchers from around the country can share ideas and coordinate approaches, for example, by developing standardized exposure questionnaires for use in epidemiological studies.

Pesticides

Identifying pesticides strongly linked to Parkinson's disease has implications for prevention and, by understanding the disease development process, researchers hope to identify treatments and points at which interventions could slow or stop the progression of the disease.

A number of studies funded by NIEHS are focused on this aspect of Parkinson's research and have yielded a treasure trove of findings. One study solved the problem of identifying pesticide exposures to specific individuals through the use of California Pesticide Use Reports and land use maps. A study in California's Central Valley found that, among the general population, exposure to the pesticides maneb and paraquat increased Parkinson's disease risk, particularly among those exposed at a young age.[2]

NIEHS-funded researchers at the UCLA School of Public Health and the University of California (UC) Berkeley School of Public Health found that combined exposure to ziram and paraquat was associated with an 80 percent increase in the risk of contracting Parkinson's disease. Exposure to those two pesticides, plus maneb, increased risk by 300 percent.[3]

Research conducted by NIEHS-funded investigators at The Parkinson's Institute and Clinical Center in California showed that pesticide applicators who used paraquat or rotenone had a more than two-fold increase in the risk of developing Parkinson's.[4]

Studies with laboratory animals have suggested that exposure to polychlorinated biphenyls (PCBs), compounds that are used in products such as transformers, may be a risk factor for Parkinson's disease. NIEHS-funded scientists at Emory University have discovered the mechanism by which PCBs may disrupt the normal functioning of dopamine.[5] The Emory researchers have also found a connection between developmental exposure to the pesticide dieldrin, a compound used for termite control in home foundations, and an increased risk of Parkinson's in laboratory mice.[6]

NIEHS grantees at Wayne State University are conducting studies on manganese, a metal that can produce neurological symptoms characteristic of Parkinson's disease at high exposure levels. Their research with laboratory mice shows that repeated manganese exposure leads to a significant loss of dopamine, a finding that may explain the mechanism underlying manganese toxicity.[7]

Genetics

An international team led by researchers at the Mayo Clinic in Florida has discovered three susceptibility genes for the development of supranuclear palsy, a rare neurodegenerative disorder that causes symptoms similar to those of Parkinson's disease. The genes do not cause the disease directly, but may make some people more or less likely to develop the disorder later in life. These gene candidates may provide clues for understanding and treating other more common brain disorders such as Parkinson's.[8]

Researchers at the NIEHS-funded Center for Gene-Environment Studies in Parkinson's Disease at UCLA have developed a genetically modified mouse that exhibits many of the cognitive deficits that are characteristic of early Parkinson's. These include deficits in maze learning, object recognition, and behavior modification. This animal model may provide scientists with new avenues for testing improved treatments for these pervasive cognitive deficits.[9]

Other researchers are studying the combined effect of environmental exposures and genetic susceptibility on Parkinson's disease risk. Studies conducted by NIEHS-funded scientists at the UCLA School of Public Health show that the risk of developing Parkinson's in pesticide-exposed individuals was greater in those who had a gene variation that affected dopamine transport than in those who did not.[10]

Researchers have also identified gene variations that are involved in protecting against Parkinson's. NIEHS investigators are studying the link between coffee drinking and a lower risk of Parkinson's disease.[11] The study found that drinking coffee protected only individuals who had a particular variation in a glutamate receptor gene. The gene involved had never before been identified as having anything to do with the disease. Finding a new gene involved in Parkinson's can have broad implications, for example, it might suggest a target for developing a new drug.

Links to Nicotine

Despite the numerous adverse health effects of cigarette smoking, a number of promising studies have looked at the curious fact that smokers seem to have a lower incidence of Parkinson's disease.

In one NIEHS-funded study, laboratory animals were treated with a compound that destroyed the dopamine-producing cells in the midbrain. Half of these animals then received nicotine in their water supply. The researchers found that the levels of dopamine transmission were greater in the nicotine-treated animals than in the controls. These findings suggest that nicotine may contribute to the lower incidence of Parkinson's in smokers.[12]

Another NIEHS-funded study worked with rats modified to have abnormal involuntary movements typical of many people with Parkinson's disease. The rats improved when injected with nicotine. This finding led researchers to conclude that smoking cessation tools, such as nicotine gum and nicotine patches, may have potential for treating the tremors of Parkinson's patients.[13]

One study by NIEHS intramural scientists found that more years of smoking, rather than the number of cigarettes smoked per day, was linked more closely to lowering risk of Parkinson's disease among smokers.[14]

No one can predict which paths of study will provide major breakthroughs. The approaches by NIEHS-funded researchers are diverse and involve experts from a wide range of disciplines. Men and women devoting their lives to this work through NIEHS and its grants include epidemiologists, gastroenterologists, neurologists, chemists, biologists, geneticists, clinicians, and experts in animal modeling and computer analysis. These new insights are moving scientists ever closer to unraveling the mysteries of this disease.

For more information on Parkinson's disease, go to our website at http://www.niehs.nih.gov.

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