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OPINION | COMMENTARY

A New Attack on Parkinson's Disease

One promising approach could also help with other neurodegenerative disorders, including Alzheimer's and Huntington's disease.

By **JON PALFREMAN**

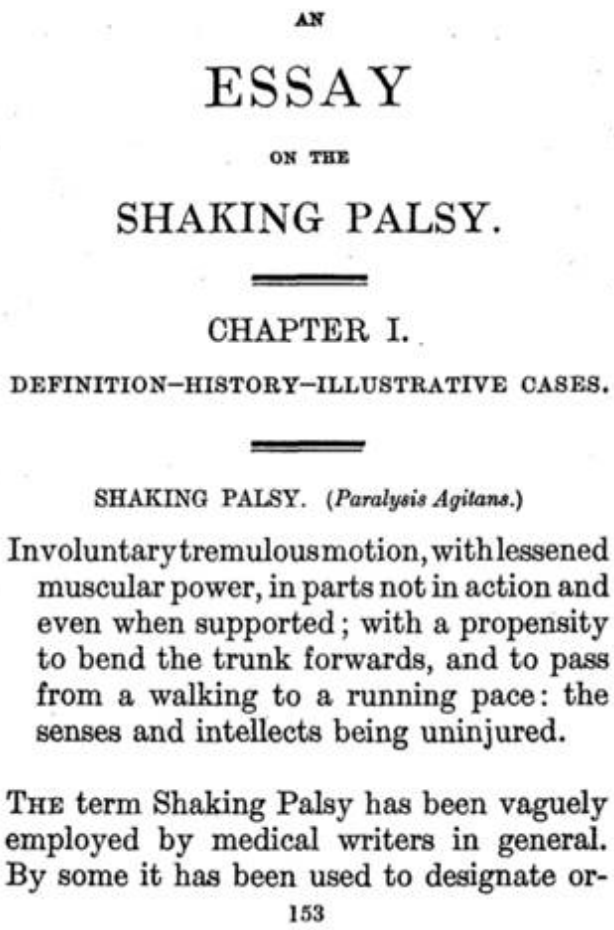
Oct. 2, 2015 7:09 p.m. ET

Walking in the east London neighborhood of Shoreditch in the early 1800s, the physician James Parkinson noticed certain individuals who moved differently from the crowd. In 1817 he articulated their symptoms, such as tremor, rigidity, slow movements and stooped gait. His "Essay on the Shaking Palsy" became the first description of what is now called Parkinson's disease. Toward the end of this classic document, Parkinson remarked in passing, "there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be stopped."

Some 200 years later, the disease, which affects one million Americans and seven million people world-wide, still hasn't been cured. While drugs such as L-dopa and surgeries such as deep brain stimulation can help manage the symptoms, all attempts to slow, stop or reverse the disease's course have failed. Efforts to protect dopamine cells with drugs, to revive dopamine cells with special growth factors and, most controversially, to graft new dopamine-making cells derived from fetal tissue into the brains of Parkinson's patients, have not panned out.

Yet recent developments have given patients like myself hope that we may be on the

verge of a breakthrough that could stop the disease as James Parkinson predicted.



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ESSAY

ON THE

SHAKING PALSY.

CHAPTER I.

DEFINITION—HISTORY—ILLUSTRATIVE CASES.

SHAKING PALSY. (*Paralysis Agitans.*)

Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured.

THE term Shaking Palsy has been vaguely employed by medical writers in general. By some it has been used to designate or-

153

The first page of James Parkinson's 1817 work, 'An Essay on the Shaking Palsy.'

Many researchers think that the bad actor in Parkinson's disease is a simple protein, called alpha-synuclein, gone rogue. The misfolded molecule forms sticky clumps called amyloids that jump from neuron to neuron killing cells. They in particular snuff out the nerve cells that make a crucial brain chemical, the neurotransmitter dopamine.

The modern picture of Parkinson's disease resembles a play in three acts. First, the alpha-synuclein-driven disease process starts, possibly in the nose or the gut, as much as 10 or 20 years before a person is diagnosed with Parkinson's. While there is not yet a definitive way to detect such early pathology, epidemiological studies show that certain symptoms—constipation, loss of smell and sleep disorders, for example—are associated with an increase in the odds of developing Parkinson's disease later.

In act two, the alpha-synuclein moves on to the mid-brain and kills off dopamine cells in a region called the substantia nigra. When 70% of these dopamine cells are destroyed, the patient starts displaying the classic tremors and other symptoms of Parkinson's disease.

In act three, the disease migrates to other brain areas such as the cerebral cortex, where it can cause hallucinations, cognitive impairment and dementia.

If alpha-synuclein is the protagonist in this story, then, reducing its levels in the brain should help control the disease. That's what researchers have been working on. A number of alpha-synuclein-busting agents are due to begin clinical trials in the next year or two. One product, developed by NeuroPhage in Cambridge, Mass., is based on a simple virus called M13. This product may be able to reduce the amounts of not only alpha-synuclein, but also the equivalent amyloids of other neurodegenerative diseases, including Alzheimer's and Huntington's disease.

Should this type of treatment work, the possibilities are extraordinary. If given early enough, such agents might prevent the development of the classic and disabling symptoms of Parkinson's disease from ever materializing. And for patients like me who already have the disease, such interventions might stop the disease in its tracks, enabling such patients to maintain our current level of health and avoid developing cognitive impairment and dementia.

Having studied the past 200 years of Parkinson's research, I am fully aware that this strategy may not succeed. Biomedical research is largely a story of failure. But from each setback comes knowledge that leads to new hypotheses. Sooner or later, we will vanquish this pernicious malady. I just hope that I'll be around to see it.

Mr. Palfreman is the author of "Brain Storms: The Race to Unlock the Mysteries of Parkinson's disease," published this month by Scientific American/Farrar, Straus & Giroux.

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