

Understanding Parkinson's More than a Movement Disorder



What exactly is Parkinson's disease (PD)? How we answer this question is not just a game of definitions, nor is it getting easier. But finding the answer is important because how we define Parkinson's is likely to be the difference between success and failure as we look for the cause(s) and for ways to combat it.

James Parkinson, the English physician who first defined the condition clinically almost two centuries ago, called it the "shaking palsy." More than a century and a half later, neurologists began to define it as one of several "movement disorders," characterized by rigidity, slowness of movement, as well as "shaking," or tremor.

The focus on motor symptoms and signs was dramatically sharpened in the 1960s by the discovery that they were due to a loss of dopamine-producing cells in the brain that make up an area known as the "nigrostriatal system" and that these motor symptoms could be improved by administration of the dopamine precursor Levodopa. Yet even at the time of this breakthrough, doctors were becoming increasingly aware that their patients were experiencing other symptoms — among them, fatigue, constipation, depression and diminished ability to smell — that seemed to be as different from one another as they all were from the movement symptoms that served as the defining characteristics of PD. Indeed, these motor symptoms have become so ingrained in the medical lexicon that we call them "parkinsonism."

What Does This Mean for Our Understanding and Management of Parkinson's?

I believe it means that we have been defining Parkinson's too narrowly, and by so doing, have been restricting our investigations too much upon one part of the brain — the dopamine-producing nigrostriatal system — at the expense of other crucial areas of investigation. Put bluntly, it is increasingly clear that "parkinsonism" — the motor

aspects of Parkinson's — is only one characteristic of what is increasingly seen as a multifaceted and complex disorder. No person who lives with Parkinson's needs to be told this. It is their reports that have been prodding specialists and researchers to look beyond the dopamine-producing nigrostriatal system to examine other areas of the brain and body.

How, in light of this complex clinical evidence, do we re-examine the scientific theory of Parkinson's? One good place to start is with F. H. Lewy, who identified a distinctive type of matter in the brains of people who die with Parkinson's called the Lewy body, the presence of which is widely recognized as the pathological hallmark of PD.

What is less widely recognized is that Lewy described these bodies not only in the nigrostriatal system, but also in other areas of the brain. Also, they have since been found in collections of nerve cells that lie just outside the spinal cord and the wall of the gut. In fact, it seems increasingly likely that Parkinson's does not begin in the nigrostriatal system, but possibly in the lower brainstem and the olfactory bulb (the part that controls ability to smell) or even the nerves in the heart and intestinal tract.

It is also becoming apparent that many of these changes outside the nigrostriatal system cause non-motor clinical symptoms that often predate the motor symptoms of Parkinson's. These are therefore often considered "predictors," or "biomarkers." I would argue that calling

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them “predictors” misses the point. The evidence is increasing that they are not just advance warnings but are actually part of the disease.

Take, for example, rapid-eye-movement sleep behavioral disorder (RBD) which is characterized by agitation and physical activity during sleep. Nearly 40 percent of men diagnosed with RBD develop Parkinson’s later in life — on average, 13 years later. In these cases, RBD is almost certainly a sign of Parkinson’s in the lower brainstem, before it has affected the nigrostriatal system and caused parkinsonism. Among people who have been diagnosed with PD, 50 to 60 percent exhibit physiological evidence of RBD, indicating that it is a common (though not universal) clinical sign of Parkinson’s.

Or take the issue of olfactory function (sense of smell). There is literature suggesting loss of smell as an early sign of Parkinson’s, with some studies showing olfactory abnormalities in up to 100 percent of people with Parkinson’s. The neuroanatomist H. Braak has observed that the olfactory sense is one of the first areas of the central nervous system to be affected by Parkinson’s and should be a part of a multifaceted diagnostic battery to detect “pre-parkinsonian” PD.

Another area of interest is autonomic dysfunction — that is, problems with bodily functions over which we have no conscious control, such as the beating of the heart, sweating or bowel function. Several studies have shown that most people with Parkinson’s experience a loss of one component of the autonomic innervation of the heart. One could speculate that fatigue, one of the most common complaints among people with Parkinson’s, might be traced to diminished heart function.

Then there is the matter of constipation, another very frequent complaint among people with Parkinson’s. First noticed by Dr. Parkinson, this problem was traditionally attributed to lack of activity, or inadequate hydration, or both. Then, in the late 1980s, scientists noticed the presence of Lewy bodies in the autonomic nervous system of the lower bowel, as well as in the esophagus. This suggests that swallowing, lower bowel and even bladder dysfunction are direct manifestations of the pathological process that underlies Parkinson’s, and in

fact may be some of the earliest features. Lending support to this hypothesis is a finding from the famous Honolulu Heart Program, a long-term study of 8,000 Japanese-American men who have been followed medically since the 1960s. The study showed that men who reported less than one bowel movement per day in midlife were more than four times as likely to develop Parkinson’s than men who reported two or more per day.

How Do We Connect These Observations?

How we proceed from here — what new studies are needed, what symptoms we should be studying, how we can connect the dots among them, whether in fact we need to rename Parkinson’s — is far from clear, and will require the attention of scientists from a variety of specialties and viewpoints. What is clear is that our concept of Parkinson’s must change, perhaps radically.

We need to broaden the clinical definition of Parkinson’s to include all of the syndromes described in this article along with depression, anxiety and others. We may either need to develop multi-disciplinary teams or to ensure that the neurologists seek more diverse training.

We also need to recognize that the observations reported have profound implications for the investigation of the causes of PD, suggesting the need for studying mechanisms of neurodegeneration that underlie the entirety of the condition, not just the part that leads to problems with movement. Knowing how the disease evolves from its inception could be hugely important in suggesting clues to its cause. The process will also have implications for efforts to modify and slow disease progression before motor symptoms have emerged.

I close by noting that none of the new dimensions of PD I have discussed will be news to scientists. What may be new is that they are coming together in compelling ways which is generating a growing interest in addressing them as a group. This will be important for the well-being of patients, the understanding of doctors and the potential of science to solve the Parkinson’s mystery.

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If you have or believe you have Parkinson’s disease, then promptly consult a physician and follow your physician’s advice. This publication is not a substitute for a physician’s diagnosis of Parkinson’s disease or for a physician’s prescription of drugs, treatment or operations for Parkinson’s disease.