

## Significance of Pathology in Neurodegenerative Disorders

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### Description

Parkinson's disease, named to recognize the contribution of James Parkinson, is the second most common neurodegenerative disease afflicting humans. Similar to Alzheimer's-type dementia, which is the most common human neurodegenerative disease, Parkinson's disease is a disorder predominantly of old age and one that is becoming increasingly common as the global population ages. In stark contrast to Alzheimer's disease, however, Parkinson's disease benefits from robust and reliable drugs to target some of the most prominent and debilitating neurological symptoms resulting from neurodegeneration. In common with Alzheimer's disease, there is yet no disease-modifying therapy available.

The clinical features of Parkinson's disease are well recognized. It is usually thought of in terms of the motor symptoms that affect hand movements and walking, but it has become increasingly apparent that nonmotor symptoms affect the majority of patients and can have a severe impact on quality of life. Like Alzheimer's disease, Parkinson's disease is a condition of age, with a mean age of onset of 60 years. Young-onset Parkinson's disease is recognized and is defined as symptoms presenting under the age of 40 years but accounts for less than 5% of cases.

It is important to distinguish between the terms Parkinsonism and Parkinson's disease. Parkinsonism is a term used to describe a group of movement symptoms, whereas Parkinson's disease implies a clinically and pathologically defined process as described in the UK Parkinson's disease Society Brain Bank criteria. This is a critical distinction: Parkinsonism, encompassing a group of symptoms, can have many causes in addition to neurodegeneration, including drugs, trauma, post infectious and vascular disease, whereas Parkinson's disease is a distinct disease entity. In many ways, this is analogous to the distinction between dementia and Alzheimer's disease and can be viewed as a semantic debate. It is however, a very important semantic difference from a therapeutic viewpoint and also when considering how we understand and categorize the molecular mechanisms underpinning the disease.

There is at present, no diagnostic test for Parkinson's disease, patients with atypical presentations may need investigations to rule out other disorders, but the diagnosis is primarily clinical, resting on the history of the patients' symptoms and findings on clinical examination, with response to therapy as a supportive phenomenon. Scans that use tracers that bind to the Dopamine Transporter (DAT) protein in the nigrostriatal nerve endings show a reduction in binding in Parkinson's disease and can be helpful in diagnosis. However DAT scan results are also abnormal in other disorders such as the atypical parkinsonism conditions and are not routinely used in diagnosis.

The three cardinal motor symptoms of Parkinson's disease are rigidity, bradykinesia and tremor. Gait and postural instability are also prominent motor features. The motor symptoms typically have an asymmetrical onset with symptoms typically manifesting initially in one upper limb. The contralateral side does eventually become involved but a degree of asymmetry tends to persist throughout the disease course.

Bradykinesia is slowness or poverty of movement and is the most fundamental feature of Parkinsonism to the extent that its presence is required for a positive diagnosis of Parkinson's disease to be made. Patients with bradykinesia will have difficulty walking with loss of arm swing and may complain of difficulty turning in bed. They may complain that their handwriting has become smaller and they have difficulties with manual dexterity. On examination, they will have loss of facial expression with mask like faces and they may notice that their voice has become quieter and more monotonous. Besides observing facial expressions and gait, bradykinesia can be examined clinically by asking the patient to perform rapid alternating movements such as tapping the forefinger and the thumb or opening the hand repetitively.

Rigidity is an involuntary increase in muscle tone with a feeling of stiffness or resistance when moving the patients' relaxed limb. Patients will complain of stiffness and will sometimes complain of aching and cramping. Rigidity can be exacerbated by asking the patient to move on the contralateral arm up and down can increase rigidity in the arm being examined. This phenomenon is known as synkinesis.

Tremor is the involuntary rhythmic oscillatory movement of a body part. Although tremor is the initial presenting symptom in about 70% of patients, 30% of patients have no tremor at all. The typical Parkinson's disease tremor is asymmetrical, most prominent at rest and increases with distraction. It is a low-frequency, 4-6 Hz, "pill-rolling type tremor" that is typically a rhythmic movement of the thumb against the index finger. Tremor of body parts, such as the chin and jaw is frequently seen in Parkinson's disease, but a full head tremor is rare. Patients with Parkinson's disease may also complain of poor balance and unsteadiness.

Besides the motor symptoms described earlier, it is increasingly recognized that Parkinson's disease is not just a motor disorder but rather, reflecting the widespread pathology of the disease has a variety of nonmotor symptoms. These symptoms can be disabling, if not more so than the motor symptoms and may present years before the motor symptoms become clinically apparent. This has led to increase interest in these symptoms as a way of predicting the onset of Parkinson's disease, which will be crucial if disease-modifying therapies become available in the future.