



## Understanding of Parkinson's disease

Parkinson's disease (PD) is the most common neurodegenerative movement disorder in the elderly. It occurs in 1% of the population over age 60 years old and 4% over 80. The mean age of onset is around 60 years, although 5-10% of patients are younger (20-50 years old). Apart from a variable age of onset, clinical symptoms also vary among patients with PD. Resting tremor is the predominant feature in some patients, while others have slowness of movement, rigidity and/or postural instability. These can occur in association with a variety of other symptoms, such as loss of smell, depression, hallucination, constipation, dry eyes, day time drowsiness, insomnia, and/or sensations of pain. In later stages of the disease, the motor symptoms become severe, and cognitive functions, such as recall & attention, can be impaired.

However, not all patients with movement problems have PD. Other motor disorders that can mimic PD include multiple system atrophy (MSA) and progressive supra nuclear palsy (PSP), and sometimes even vascular problems in the brain can cause similar movement difficulties<sup>1</sup>. A patient with a clinical diagnosis of PD needs to be followed for a certain period of time to determine which of these disorders<sup>1</sup> are responsible, as the same regions of the brain can be damaged by different pathologies<sup>2</sup>.

The diagnosis of PD is often a shock, and patients want to know more about the disease, its cause, any treatments, and overall what the future will hold.

The causes and course of PD differ among individuals. In general, these are determined by a complex interaction between genetic and environmental factors.

In terms of genetic causes, PD can run in families (known as familial PD), but usually not every child with a parent affected inherits the disease, and occasionally people with an inherited genetic mutation causing PD do not get the disease. In some families a phenomenon of earlier disease onset in younger compared to older generations has been observed<sup>3</sup>. The first gene causing familial PD was identified in 1997, called alpha-synuclein<sup>4</sup>. The alpha-synuclein gene encodes a small protein with important function involved in learning and neurotransmission. There are now many other genes known to cause PD<sup>5</sup>. In Australia, the most common genetic cause is variations in a gene called LRRK2<sup>6</sup>.

For the majority of patients with PD, no other family members are affected (known as sporadic PD). For those with sporadic PD, normal genetic variation plays a role in both the risk of developing the disease<sup>5</sup> and the rate of its progression<sup>7</sup>. Some patients with PD experience slow disease progression with only minor movement impairment over decades,



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while others experience fast disease progression with severe disability within 5-10 years. Recently, we found that different variations in the alpha-synuclein gene and another gene known as the microtubule-associated protein tau (MAPT) gene can influence the speed of clinical deterioration in PD<sup>7</sup>. Assessment of genes extracted from a blood sample allowed us to predict the rate of disease progression with a 94% accuracy in a subpopulation, a finding recently confirmed by another study in a different population of patients<sup>8</sup>.

In terms of environmental factors impacting on PD, exposure to certain toxins is a risk factor for developing PD<sup>9</sup>. Recent evidence suggests that some viral infections may compromise the immune system and could precipitate the onset of PD<sup>10</sup>. However, knowledge on the relative risks of environmental versus genetic factors remains uncertain, and how these factors interact needs to be evaluated. Such research is likely to hold the key to cure this devastating disorder.

■ Written by Dr. Yue Huang

As a researcher focus on Parkinson's disease, I feel that my understanding on Parkinson's disease is so limited.

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