## **Parkinson's Disease**

One percent of people over 60 and 4% of people over 80 have Parkinson's disease. Of all neurodegenerative diseases, Parkinson's disease is second only to Alzheimer's disease in prevalence, with 5 million people worldwide having the condition. The characteristic pathological feature of Parkinson's disease is the degeneration of dopaminergic neurons in a deep part of the brain called the substantia nigra pars compacta (SNc). The SNc is part of the basal ganglia, an old part of the brain responsible for regulating movement and some aspects of cognition. Clinical features of the disease are tremor (shaking), rigidity and slow movement (bradykinesia). As the disease progresses, other symptoms such as gait disturbance, falls and cognitive impairment can also appear.

There is no cure for Parkinson's disease, but there are medications that are available for partial (or sometimes nearly complete) relief of symptoms during the early-stages of the disease. The later stages are often poorly responsive, or even unresponsive, to any medical treatment. Fortunately, deep brain stimulation (DBS) is a surgical procedure that has had some extraordinary success in treating patients for whom medicine has failed. In DBS, electrodes are implanted deep in the patient's brain to provide small stimulating electric currents to specific brain regions. It is unknown how these electric currents work, but in some cases they work so well that patients can once again walk well and live normal lives. If stimulation is turned off, symptoms return, sometimes immediately but usually within a couple of hours.

The primary symptoms of Parkinson's disease are:

Tremor: Tremor is the most common and well-known symptom, usually appearing in the hands or feet first, often on one side before spreading to unaffected limbs. Most cases of the disease, around 70%, start with tremor as the first major clinical symptom (although loss of smell often precedes it).

Rigidity: Rigidity is caused by continuous involuntary contraction of the muscles. It typically starts in the neck and shoulder muscles before spreading to the face and limbs, making it difficult to move.

Bradykinesia: Bradykinesia is slowness in planning and executing movements, and is usually the most disabling symptom in early Parkinson's disease. Performing multiple movements simultaneously and stringing movements together is particularly difficult.

Postural instability and freezing of gait: These symptoms appear in late-stage Parkinson's disease. Postural instability is an inability to maintain an upright posture, leading to poor balance. Freezing of gait is impaired ability to initiate and maintain walking and to change direction when walking, leading to frequent falls. These symptoms typically do not respond to current medications and, if severe and impacting quality of life, are good candidates for DBS.

Various other symptoms can also appear, including tingling and numbness, sleep disorders leading to drowsiness and insomnia, autonomic nervous system disorders leading to such symptoms as low blood pressure, undue sweating, incontinence and constipation, and ocular problems such as dry eyes and double vision. Neurological disorders and cognitive problems such as inability to think flexibly or abstractly, poor impulse control, poor memory and short attention span are also quite common. Dementia is up to 6 times more likely in Parkinson's disease patients.

Treatment of early-stage Parkinson's disease is usually with Levodopa (L-DOPA), which adds dopamine to the SNc and therefore relieves some of the motor symptoms. Long-term treatment with L-DOPA eventually results in complications (dyskinesia, or involuntary movements and writhing of the body) so its use is often delayed as long as possible. Other medications can sometimes be used instead to either replace L-DOPA or allow a lower dose of L-DOPA to be administered. Late stage PD can sometimes be treated with DBS. DBS does not always work, but when it does the symptomatic improvement can be remarkable. However it is major surgery and the expected improvements need to be weighed against the risk.