Atypical Parkinsonism

What is “Typical” Parkinson's Disease?

Parkinson's disease (PD) is a progressive brain disorder which usually produces some combination of the following symptoms:

1. Tremor at rest.
2. Slowed movement.
3. Stiffness or rigidity of muscles.
4. Unsteadiness when standing or walking.
5. "Freezing" or sudden loss of ability to move (as if the feet are "glued" to the floor).

PD results from the dying off (degeneration) of certain nerve cells found in a deep part of the brain (brain stem) called the substantia nigra. The reason for the cell death is not exactly known but is thought to be due to the accumulation of a protein called alpha-synuclein – which is why PD is considered a “synucleinopathy”. These cells produce a neurotransmitter chemical called dopamine. It is the depletion of dopamine in the brain that results in the symptoms of PD. Initially, Parkinson's disease symptoms improve with dopamine replacement in the form of levodopa (Sinemet). Although the dopamine producing nerve cells in the substantia nigra are dying, the nerve cells in the basal ganglia (striatum) which are normally stimulated by dopamine, have well preserved dopamine receptors and continue to respond. The cornerstone of medical treatment of PD is administration of levodopa, which is taken up and converted into dopamine by the brain.

“Atypical” Parkinsonism and How It Differs from Parkinson's Disease

Parkinsonism refers to a set of symptoms typically seen in Parkinson's disease but caused by other disorders. Atypical parkinsonism includes a variety of neurological disorders in which patients have some clinical features of PD, but the symptoms are caused not only by cell loss in the substantia nigra (the brain area most affected in classic PD), but also by added degeneration of cells in the parts of the nervous system that normally contain dopamine receptors (striatum). In other words, the patients look like they have PD, but the cause of their symptoms is different from that of “classic” PD. Patients with atypical parkinsonism have symptoms like PD, including resting tremors, slowed movement, stiffness, gait difficulty and postural instability, but have additional symptoms and signs that are not typically present in PD. This had led to the commonly used term “Parkinsonism
plus syndrome”. A few such syndromes that are well described and, like PD, are thought to be related to the abnormal accumulation of proteins such as alpha-synuclein (“synucleinopathy”) or tau (“tauopathy”).

The additional symptoms and signs may include inability to look up and down (vertical gaze palsy) and early postural instability leading to frequent backward falls, such as seen in progressive supranuclear palsy (PSP – a tauopathy), the most common form of atypical parkinsonism. Patients with PSP often have the “procerus sign” which is a particularly “worried” facial expression. The second most common form of atypical parkinsonism is multiple system atrophy (MSA – a synucleinopathy). Patients with MSA are typically distinguished from those with PD by the presence of autonomic features such as unstable blood pressure (particularly orthostatic hypotension, which refers to drops in blood pressure when standing), early disturbance of sexual, bladder, and bowel dysfunction, reddish-blue discoloration of skin (the "cold hand" sign), and marked sleep disturbance (e.g. acting out dreams and sleep apnea). Other typical features of MSA include forward head tilt (anterocollis) or a body tilt when sitting (Pisa sign), loss of coordination, and a rapidly progressive course with inability to ambulate usually within the first 3-5 years of onset. MSA is divided into MSA-C (cerebellar variant) which has more symptoms of ataxia (incoordination) and MSA-P (parkinsonian variant) which has more parkinsonian symptoms but is unresponsive to the usual therapy for Parkinson's disease (levodopa).

Other forms of atypical parkinsonism are Dementia with Lewy bodies (DLB – a synucleinopathy) and corticobasal syndrome (CBS – a tauopathy). Patients with DLB have, in addition to the parkinsonian features, early dementia (usually preceding or co-occurring with the parkinsonian symptoms) and visual hallucinations (seeing people, small animals or objects that are not real) with their symptoms typically fluctuating leading to “good days” and “bad days”. Patients with CBS usually present with asymmetric stiffness, apraxia (inability to carry out learned purposeful movements), alien limb (the hand or the leg seem to have "a mind of their own"), and limb dystonia (abnormal sustained muscle contractions causing abnormal postures and twisting) or myoclonus (sudden jerking).

Another common cause of atypical parkinsonism is “vascular parkinsonism” caused by multiple and usually very small strokes. These patients tend to have more symptoms in the lower extremities (lower body parkinsonism) with walking difficulties, balance problems and falls.

The various atypical parkinsonian syndromes are classified according to the patterns of damage they produce in the nervous system, the constellation of clinical symptoms they cause, and their natural course (see Table 1. Parkinsonism Plus Syndromes: Differential Diagnosis.)

Poor or no response to levodopa is a common feature to all forms of atypical parkinsonism. In contrast to typical PD, in which dopamine receptors are spared,
patients with atypical parkinsonian disorders have lost their dopamine receptors and therefore they do not respond to levodopa as well as those with typical PD. This can be demonstrated by special imaging such as positron emission tomography (PET) and dopamine transporter imaging (DAT-SPECT). MRI may be also helpful in differentiating PD from atypical parkinsonism.

There are probably many causes of atypical parkinsonism, but no one specific cause has been identified. Usually only one member of a family is affected and, therefore, these disorders are thought to be sporadic and not inherited. There is much active research into the causes of these disorders.

How to Support Research

Because the various atypical parkinsonism diseases are relatively uncommon, it is difficult to obtain public funding for research. Therefore, research into these disorders largely depends upon private contributions, particularly from patients and families affected with the diseases. Besides financial support and willingness to participate in clinical research projects, scientists are interested in examining postmortem brains of patients who were afflicted with these disorders. To arrange for a brain donation to a qualified “brain bank” you should contact your neurologist or the National Parkinson Foundation for further information.

Support Groups for Patients and their Families

Patients affected with atypical parkinsonism and their families should consider joining national or local support groups. Membership in these organizations facilitates exchange of information that may be useful in coping with the physical and mental disabilities associated with these disorders. Also, many local support groups offer exercise therapy which may be helpful to some patients. With the emotional support of family members and expert medical management guided by knowledgeable and compassionate physicians, many patients with atypical parkinsonism can lead enjoyable and productive lives.

Selected References


Helpful organizations

**CurePSP: Foundation for PSP, CBD and Related Brain Diseases**

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3rd Floor
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**Multiple System Atrophy Coalition™**
[https://www.multiplesystematrophy.org/](https://www.multiplesystematrophy.org/)

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**Multiple System Atrophy Trust**
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