

DYSTONIA AND PARKINSON'S DISEASE

Despite its prevalence, dystonia is under-recognized and therefore undertreated.

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Dystonia is the third most common movement disorder, after essential tremor and Parkinson's disease (PD). Despite its prevalence, it is under-recognized and therefore undertreated.¹ Even patients with cervical dystonia, the most frequent form of isolated adult-onset focal dystonia, may see multiple providers over the course of longer than a year until accurate diagnosis is made and optimal therapy prescribed.² The combination of unique signs and symptoms, and lack of familiarity among physicians and patients alike can lead to missed or incorrect—including psychogenic—diagnoses.

Defining and Describing Dystonia

The term dystonia is used to describe abnormalities of motor control causing sustained or intermittent muscle contractions, resulting in repetitive postures or movements. These are usually consistently directional in nature. They are frequently twisting or turning movements and can be tremulous.³ Dystonia may be precipitated or worsened by voluntary action, such as walking or running. There may be a sensory trick, or "geste antagoniste" whereby a light touch, or the thought of a movement, may quiet the dystonia.

Dystonia can strike different body parts—the eyes (blepharospasm), lower face (oromandibular dystonia), voice (spasmodic dysphonia), neck (anterocollis, laterocollis or retrocollis), torso (truncal dystonia, camptocormia, pleurotonus), or extremities (limb dystonia or writer's cramp in the arm). Infrequently, it may be specific for certain activities, such as with musician's dystonia or golfer's yip. It may affect only one region or may be generalized. The pulling and twisting

movements are not always associated with discomfort but dystonia may cause pain, and the posturing may significantly interfere with normal function and diminish quality of life.⁴

Characterizing Dystonia

Consensus criteria for the classification of dystonia were refined in 2013 and involve assessment of two axes:

- 1.) Clinical characteristics:** age at onset, body distribution, temporal pattern, and associated neurological or systemic features, and
- 2.) Etiology:** nervous system pathology; pattern of inheritance, if any; mechanism of acquisition.³

This is where neuroimaging, genetic testing and/or medication review would enter in the appropriate clinical scenario. Imaging might evaluate for stroke; genetic testing may be done for DYT1 or

Wilson disease; and past use of typical or atypical dopamine antagonists could be reviewed.

Dystonia in Parkinson's Disease

Dystonia may exist as a distinct condition, as in the case of “isolated dystonia,” in which there are no other neurological symptoms. Conversely, it can occur as just one feature of a more complex syndrome, such as atypical parkinsonism or idiopathic PD. Within Parkinson's, dystonia can be the presenting sign, an associated symptom of the disease or temporally correlated with levodopa administration. The latter is the most typical demonstration of dystonia in Parkinson's disease.⁵

Dystonia as a Presenting Symptom of Parkinson's

Dystonia is not a classic presenting symptom of PD. However, because isolated lower limb dystonia uncommonly starts later in life, adult onset of such should raise concern for idiopathic Parkinson's disease.^{6,7} Kinesigenic foot dystonia—toe curling or foot inversion while exercising—has been reported among those with younger-onset disease, which is diagnosed prior to age 50.^{8,9} The lower extremity is the usual region afflicted by dystonia in Parkinson's. Patients experience great toe dorsiflexion or foot inversion and/or plantar flexion, both of which can impair gait and cause cramping and aching pain.¹⁰

Other possible manifestations of dystonia in Parkinson's are blepharospasm, bruxism, anterocollis, torticollis, upper extremity flexion and adduction, camptocormia, pleurotonus (Pisa syndrome), and anismus.^{5,11,12} A few of these are explored in more detail below.

Blepharospasm

Although more common in atypical parkinsonism, blepharospasm can be seen in patients with idiopathic Parkinson's disease.¹³ This focal dystonia is characterized by involuntary contractures of the orbicularis oculi that result in sustained eye closure. It is often preceded by an increased rate of blinking and coupled with a sensation of eye irritation and photophobia. Blepharospasm can be paired with apraxia of eyelid opening—an inability to open the eyes due to failure of levator palpebrae contraction. These conditions vary from annoyances that interfere with reading and watching television to severely disabling disorders that render one functionally blind and preclude driving. The treatment of choice for blepharospasm is chemodenervation with botulinum toxin injections into the

orbicularis oculi muscles.¹⁴ For patients who decline injections or experience incomplete relief with this treatment, oral medications—namely benzodiazepines, anticholinergics or spasmolytics (baclofen)—may be effective. Adjustments to dopaminergic therapy may be beneficial if symptoms worsen with wearing off in PD. Lubricant eye drops or ointments can be soothing for the sensation of eye irritation. Eyelid crutches or Lundie loops (glasses fitted with wire loops to press against the brow) may keep the lids open in the case of apraxia or serve as a sensory trick in blepharospasm.¹⁵

Anterocollis

Anterocollis refers to forward flexion of the neck out of proportion to trunk flexion. Some view it as a red flag for multiple system atrophy but it can occur in idiopathic PD and, perhaps, might simply indicate an axial form of the disease.¹⁶ Severe anterocollis results in an inability to lift the head off of the chest. Dysphagia, dysarthria and sialorrhea are often aggravated as a result. It can interfere with vision and gait, and understandably lead to pain. Supportive measures for the latter may include a soft cervical collar; physical and occupational therapy; and, in select patients, muscle relaxants. If anterocollis occurs exclusively as an “off” phenomenon, optimizing dopamine therapy should be the initial management. Movement disorders specialists may inject botulinum toxin into the bilateral anterior scalene and/or sternocleidomastoid (SCM) muscles, but with caveats. While side effects of botulinum toxin therapy may be minimized by utilizing EMG guidance and injecting the upper one-third of the SCMs, dysphagia in particular remains a significant risk. Surgical fusion of the cervical spine and deep brain stimulation (DBS) are occasionally effective. Anterocollis, especially when out of proportion in severity to other symptoms and present early on, should not automatically be attributed to idiopathic Parkinson's—atypical parkinsonism, namely multiple system atrophy, should be considered. Furthermore, when neck extensor weakness is present, other diseases—inflammatory myopathy, myasthenia gravis or motor neuron disease—should be excluded.^{17,18}

Camptocormia and Pleurotonus

Camptocormia and pleurotonus affect the torso—the former causes extreme anterior flexion (>45°); the latter is a lateral flexion and backward axial rotation. Both resolve upon lying supine and camptocormia also straightens with standing up against a wall, meaning the deformities are not fixed. This is in contrast to the spinal compression fractures, degenerative disc disease and scoliosis (lateral curvature of the spine) that many times occur in conjunction



with and exacerbate these conditions. While there may be debate as to whether these are purely dystonic conditions (or if camptocormia represents a myopathy),¹⁹ most agree there is at least some element of dystonia that varies in severity in individual patients. If camptocormia and pleurotonus do present in idiopathic PD, they generally come on subacutely at least 7-8 years into the course of disease. People with camptocormia describe sensations of being pulled forward, abdominal tightening, lower back pain and/or dyspnea. Pleurotonus causes patients to initially tend to lean to one side while sitting and eventually this occurs while ambulating as well. They, too, complain of pain and dyspnea. These irregular postures interfere with mobility and vision and lead to gait instability and falls.¹⁷ As a general rule, camptocormia and pleurotonus are not dopamine-responsive. Treatment regimens are inconsistent and somewhat disappointing. Options include physical therapy; anticholinergic medications in younger patients; and botulinum toxin injections into dystonic musculature (rectus abdominis, iliopsoas or paraspinal muscles—depending on EMG and physical examination findings). DBS of the subthalamic nucleus (STN) or globus pallidus internus (GPi) provides relief in select patients. Spinal fusion surgery has been employed in medically-refractory cases but the risk of complication and need for revision is high. Orthotics and other devices can be worn to bring the stance more upright; however, caution must be exercised to not too suddenly overcorrect the posture and increase the chance of falling.¹⁷ Assistive devices minimize flexion, provide a sensory cue that transiently improves posture, and decrease fall risk.⁵

Remember the Differential Diagnosis

The most likely explanation for each of the above dystonias in a person with Parkinson's disease is the underlying neurodegenerative disorder. Still, other illnesses can arise concurrently. When symptoms come on acutely, the practitioner must look for metabolic changes, infectious causes, and structural or vascular etiologies, to name a few. A critical review of the medication list is always worthwhile—neuroleptics, anti-emetics, antidepressants, lithium, valproate, cholinesterase inhibitors, and even dopamine agonists (many of which are prescribed in advanced Parkinson's) have all been reported to induce these dystonic syndromes.^{17,20} Finally, when any dystonia appears in the first few years of a suspected idiopathic PD, specifically if it is significant, rapidly progressive, and non-dopamine responsive, one must consider an atypical parkinsonian syndrome in the differential diagnosis.

Dystonia in the Context of Levodopa Use

The majority of patients with Parkinson's take levodopa at some point in the course of their disease. Long-term use of this drug and disease progression are often accompanied by motor complications, which consist of motor fluctuations and dyskinesia.²¹ The former involve a return of parkinsonian signs and symptoms—slowly as medication wears off at the end of a dose, or suddenly, randomly, or unpredictably (as when individual medication doses fail to take effect). Dystonia can be a prominent part of these “off” periods but can also punctuate times when patients are “on” and medication may otherwise be working well.

Specific considerations for medication adjustments are described for the respective situations in which dystonia occurs below. If the symptoms are severely disabling and not remedied with medication changes, though, DBS may be an option. Surgery may improve “off” and early morning dystonia by providing continuous stimulation. It may alleviate peak-dose and diphasic dystonia by allowing dopaminergic medications to be lowered. While the GPi is the most standard target for isolated dystonia, it is not clearly more advantageous than STN for dystonia in Parkinson's. As compared to DBS of GPi, however, that of the STN has been associated with a potentially greater reduction in dopaminergic dose, and this may be beneficial in the management of “on” phase dystonia.

“Off” Dystonia

When dystonia emerges in the context of chronic levodopa usage, it is most often in the “off” state and appears ipsilateral to the more severely parkinsonian side. This is when dopamine levels are low, as medication is wearing off at the end of dose or during the nighttime.^{5,22} Initial steps to combat wearing off dystonia typically involve increasing the levodopa dose and/or frequency of administration. Otherwise, the general management centers on longer-acting strategies like COMT-inhibitors, MAO-B inhibitors, and/or extended-release formulations of carbidopa/levodopa or dopamine agonists. Potential adverse effects, such as dyskinesia, must always be taken into account. For some patients, benzodiazepines or anticholinergics may be helpful. In the case of severe “off” dystonia, botulinum toxin injections may be required.²³

Early Morning Dystonia

This dystonia surfaces in the early morning hours, before the first dose of levodopa has taken effect. It most often impacts one or both of the lower extremities. It can last until the daytime medication kicks in or may spontaneously resolve. Symptoms can be mitigated with an



immediate-release formulation of levodopa, injection of apomorphine, and/or an extended-release formulation of a dopamine agonist.^{5,22}

Peak-Dose Dystonia

Dystonia may also occur during “on” periods. At peak-dose, when plasma dopamine levels are highest, motor function is optimal or complicated by dyskinesia.^{5,22} If dystonia happens during this time, levodopa dose may need to be decreased and the drug given more frequently. Amantadine may also aid in improving dyskinesia.

Diphasic Dystonia

Rarely, patients may exhibit a diphasic pattern of dystonia during both the “on” and “off” states. In this scenario, dystonia occurs when plasma dopamine levels are actually rising or falling rather than when they are at the trough or peak.^{5,22} Clinically, dystonia manifests at the beginning and end of a medication dose.²¹

Diphasic dystonia represents a particularly difficult management issue. Attempting to lower the peak dopaminergic medication dose and employing the longer-acting medication tactics discussed for “off” dystonia are standard approaches. Patients who remain

levodopa responsive but are plagued by intolerable drug side effects may be considered for DBS as discussed above.

Medication titration in each of these situations is obviously individualized. It is a trial and error process and communication between the patient and physician is paramount. The clinician must first determine when in the cycle of medication administration dystonia is occurring and the patient’s assistance is often necessary to chart this out. Sometimes this requires that the patient videotape or mimic their symptoms so that dystonia and dyskinesia can be correctly identified. Doing so ensures that the patient and physician are speaking the same language and discussing the same symptoms so that ideal medication adjustments can be made.

Dystonia in and of itself can be complicated to diagnose and manage, not to mention frustrating to live with on a daily basis. Adding Parkinson’s only makes it more challenging. Increasing awareness of dystonia among clinicians, patients, and society as a whole will hopefully translate to improved treatment and therefore overall quality of life for people with dystonia and Parkinson’s disease.

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The Michael J. Fox Foundation is the largest nonprofit funder of Parkinson’s disease research worldwide. The Foundation is dedicated to finding a cure for Parkinson’s disease through an aggressively funded research agenda and to ensuring the development of improved therapies for those living with Parkinson’s today. Because patients are vital partners in this process, the Foundation works to mobilize volunteer engagement in research by providing education and direct research-related services to Parkinson’s clinicians, researchers, patients and families.



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