

Postural deformities in Parkinson's disease



Karen M Doherty, Bart P van de Warrenburg, Maria Cecilia Peralta, Laura Silveira-Moriyama, Jean-Philippe Azulay, Oscar S Gershanik, Bastiaan R Bloem

Postural deformities are frequent and disabling complications of Parkinson's disease (PD) and atypical parkinsonism. These deformities include camptocormia, antecollis, Pisa syndrome, and scoliosis. Recognition of specific postural syndromes might have differential diagnostic value in patients presenting with parkinsonism. The evidence to date suggests that postural deformities have a multifactorial pathophysiology. Contributing factors include muscular rigidity; axial dystonia; weakness caused by myopathy; body scheme defects due to centrally impaired proprioception; and structural changes in the spine. The relative contribution of these different factors varies between patients and across specific syndromes. Improved understanding of the mechanisms underlying postural deformities in PD might ultimately lead us to more effective management strategies for these disabling and drug-refractory complications.

Introduction

Patients with Parkinson's disease (PD) or atypical parkinsonism often present with abnormal posture. A retrospective observational study showed that a third of patients with PD had a deformity of their limbs, neck, or trunk.¹ The most recognised type of deformity is the classic stooped simian appearance, with flexion of the hips and knees, and rounding of the shoulders (figure 1). An important subset of patients shows more severe abnormalities of posture or spinal alignment, leading to significant disability. These severe postural deformities include camptocormia, antecollis, Pisa syndrome, and scoliosis. The underlying pathophysiology of these deformities is largely unknown, and their management remains difficult.

This Review provides an update on the prevalence, clinical presentation, and treatment of the axial postural deformities encountered in Parkinsonism. The possible pathophysiological mechanisms are reviewed, and areas that require further study are emphasised. Most patients present with a combination of deformities in both the sagittal and coronal plane (figure 2). We separate them according to the predominant plane of deformity. The striatal hand and foot deformities have been covered in a previous review.² We therefore limited our analysis to articles related to deformities of the axial skeleton.

Sagittal plane deformities

Camptocormia

Definition

James Parkinson first described the stooped or bent posture of patients with PD (figure 1).³ The term camptocormia is used to describe a distinctive and much more pronounced manifestation of this stooped posture, with flexion originating in the thoracic or lumbar spine (figure 2A and figure 3). Camptocormia is also referred to as bent spine syndrome, a term used in the past to describe soldiers who developed a persistently bent spine as a manifestation of what we now call post-traumatic stress disorder.⁴ There are no consensus criteria for diagnosing camptocormia. Most authors have used an arbitrary figure of at least 45° thoracolumbar flexion apparent when standing or walking, but which resolves

when the patient lies supine.^{1,5,6} More often, the diagnosis is made by subjectively assessing the patient's posture.

Epidemiology

The term camptocormia was first used to describe bent spine in a patient with PD in 1999.⁷ Four subsequent studies described prevalence rates in PD of between 3% and 17.6% (table).^{1,6,8,9} This wide range probably reflects the different thresholds that physicians use for diagnosing camptocormia, the lack of a clear clinical definition, and the different populations studied. Epidemiology studies suggest that the prevalence of camptocormia might be higher in Asian patients,⁸ which might reflect a genetic difference in skeletal shape between different ethnic groups. Most reports show a positive association between camptocormia and disease severity, with patients with camptocormia tending to have more advanced parkinsonism than those without.^{1,6,21,22} Patients with camptocormia also tend to be older.⁷ On average, camptocormia presents 7–8 years after the onset of parkinsonism.^{5,7,9,21–23}

Clinical presentation

Patients might not complain about their abnormal posture until it interferes with their mobility or vision, especially if onset of the deformity was gradual. In some patients the onset is subacute, with development of significant flexion over days to months.^{9,21,23} Back pain is common, and it is often associated with a previous history of back problems, degenerative spinal disease, or surgery,^{5–7,21,22} but it is not clear whether this association is a risk factor in the development of camptocormia. Some patients report a feeling of being pulled forward, or a sensation of tightening in their abdomen.⁵ Posture is often reported to deteriorate further on walking or if patients undertake strenuous physical activity.²¹ If the deformity is long established with secondary fixed changes, patients might complain of breathlessness due to restricted lung capacity, or of difficulty lying flat in bed due to hip or knee contractures; the latter can be accompanied by skin irritation in the flexed segment.²²

Examination can reveal a fully reversible deformity that patients can overcome when asked to stand up straight

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Reta Lila Institute of Neurological studies, UCL Institute of Neurology, Queen Square, London, UK (K M Doherty MRCP, L Silveira-Moriyama PhD); Department of Neurology and Parkinson Centre Nijmegen, Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen Medical Centre, the Netherlands

(B P van de Warrenburg MD, Prof B R Bloem MD); Cesar Milstein Hospital, Department of Neurology and Movement Disorders Clinic, Buenos Aires, Argentina (M C Peralta MD); Service de Neurologie et Pathologie du Movement, Hôpital de la Timone, Marseille, France (Prof J-P Azulay MD); and Institute of Neuroscience, Favaloro Foundation University Hospital, Buenos Aires, Argentina (O S Gershanik MD)

Correspondence to:

Prof Bastiaan R Bloem, Parkinson Center Nijmegen, Department of Neurology (935), Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, the Netherlands
b.bloem@neuro.umcn.nl

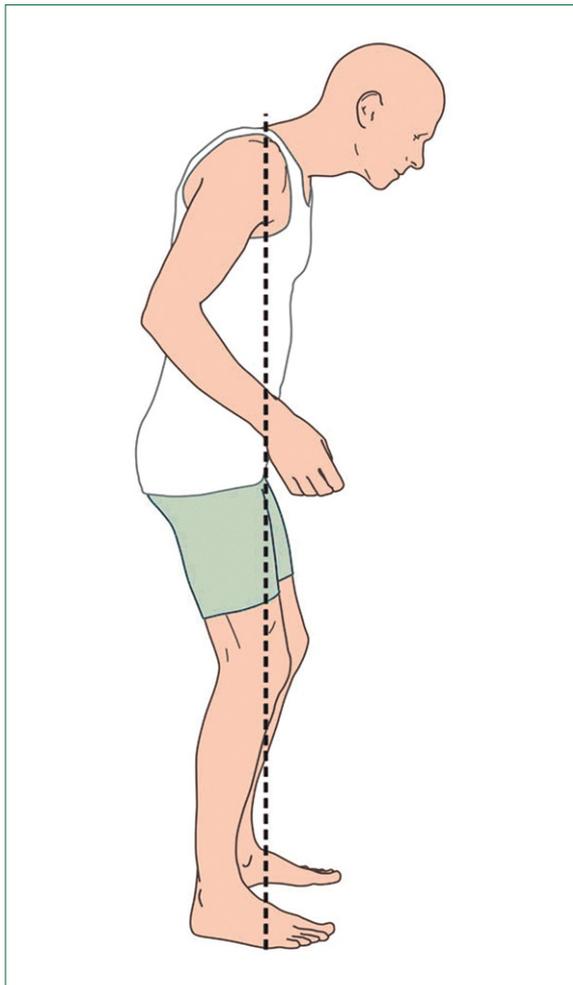


Figure 1: The classic 'stooped' appearance of PD with mild hip and knee flexion and rounding of the shoulders

See Online for webvideos

(webvideo 1) or stand against a wall, but in others the abnormal posture is more fixed, and cannot be corrected until the patient lies flat (webvideo 2, figure 3). Some believe that the manoeuvre of standing against a wall to enable erect posture represents a *geste antagoniste* or sensory trick, but it might be that this is simply a safe surface against which patients can attempt to stand as straight as possible without the risk of falling backwards. Neurological examination often reveals marked axial rigidity.^{9,22} Strength of trunk and hip extension are normal unless testing is precluded by fixed posture or pain.⁹ The paraspinal muscles can have a wooden consistency, and the rectus abdominis often feels tense.⁵ There might be compensatory hyperextension of the neck to obtain a normal visual field. There is often mixed deformity, with deviation also in the coronal plane.

Differential diagnosis

Diagnosing camptocormia in the setting of parkinsonism is based on clinical examination alone, as aetiological

investigation of the deformity is hindered by the paucity of knowledge in this area. Nevertheless, some specific findings might suggest alternative diagnoses. For example, weakness of truncal extension suggests concomitant myopathy or anterior horn cell disease, and should trigger further focused investigations. Fixed deformity that persists even when supine implies osteoarticular changes, which can either be causative (eg, vertebral fractures, ankylosing spondylitis) or be secondary to the deformity (eg, acquired degenerative spondyloarthropathy). A list of differential diagnoses and tailored ancillary investigations is shown in figure 4.

Treatment

It is generally accepted that camptocormia is not a levodopa-responsive phenomenon,^{5,7} although one author reported a modest improvement in forward flexion when patients were in the on-drug state, as opposed to the off-drug state.²² It also seems that patients with PD with camptocormia are sometimes less responsive to levodopa than those without this deformity, and have fewer levodopa-induced limb dyskinesias.²² This might be because camptocormia is associated with a more severe parkinsonian phenotype (postural deformity variant parkinsonism), or it might simply reflect long-standing disease for which drug treatment results in a less effective on state. More detailed studies with larger numbers are needed to clarify this finding.

Anticholinergic drugs can be prescribed for their anti-dystonic properties in patients under the age of 65 years, but there is no evidence to support their use. Botulinum toxin injection to the rectus abdominis, iliopsoas, or selected paraspinal muscle groups has been used, mainly in patients deemed to have a predominantly dystonic element to their deformity. Azher and Jankovic have found this successful in selected patients,⁵ but few have reproduced their positive results.^{24,25}

Deep brain stimulation (DBS) of both subthalamic nuclei is a potential treatment for camptocormia in PD, but outcomes have varied from excellent improvements^{26–28} to only mild improvement or no benefit.^{29,30} The pallidum is another potential target to treat camptocormia caused by idiopathic axial dystonia,²⁹ but previous research on patients with PD with camptocormia is limited to only five cases, with no improvement to the posture reported in two, and modest improvement of posture in three.^{29–32} There is interest in the pedunculopontine nucleus (PPN) as a potential stimulating target in patients with PD, but the evidence is more specific for freezing of gait and postural instability, rather than postural deformity.^{11,33,34} In our view, camptocormia should not yet be regarded as a specific and separate indication for DBS in patients with PD.

Spinal surgery has been used to correct postural deformity in patients with PD, in particular when medical measures have failed. This approach has significant

complications, and often requires revision surgery, although posture improves in some.^{19,35–38}

Other treatments for camptocormia include focused manipulative physiotherapy, hydrotherapy, and the use of abdominal binders, corsets, or spinal braces (orthotics), but these measures are rarely successful for a sustained period, and have little-to-no evidence base. Care must be taken not to cosmetically overcorrect the stooped posture, as a sudden or uncompensated change to sagittal balance could increase the risk of falling backwards.³⁹ de Sèze and colleagues⁴⁰ report the use of a spinal orthotic device that aims to induce a lumbar lordosis in patients with camptocormia. The outcomes in the five tested patients with PD were good in terms of improvements in quality of life, pain, and sagittal balance. Follow-up radiography showed an improved lumbar lordosis. Patients wore the orthotic device on average for 7 h per day, which suggests that good outcomes might be contingent on the motivation and compliance of the patient. There is a single report of a patient whose camptocormia was completely relieved when he wore a low-slung backpack.²⁵ This might be a more attractive option for patients who do not want to wear a spinal brace. General therapeutic options for the various postural deformities are suggested in figure 4.

Antecollis

Definition

Antecollis in parkinsonian disorders refers to a forward flexion of the head and neck. When mild, this might be seen as part of the stooped posture in patients with PD, but some patients present with what is called a disproportionate antecollis: neck drop that is more pronounced than expected relative to the flexed posture of the trunk and limbs.^{41,42} The term dropped head syndrome is sometimes used to describe marked neck flexion, but is more often reserved for neuromuscular disorders such as myasthenia gravis, polymyositis, and motor neuron disease,⁴³ in which it is associated with weakness of neck extension (literally causing the head to drop forward).

Epidemiology

Antecollis has been recognised only recently as a feature of parkinsonism.⁴⁴ It is said to be a relatively common feature of multiple system atrophy (MSA) in which the antecollis is relatively fixed, unlike in idiopathic spasmodic torticollis.⁴¹ Ashour and Jankovics⁴¹ retrospective study quotes a high prevalence of 42·1% for this deformity in patients with MSA, whereas the average figure is much lower at 5·8% in PD.^{11,10–12} In a series of 15 patients with PD, antecollis was more often found in women and in patients whose prominent parkinsonian signs were rigidity and akinesia.¹¹ As with other postural deformities, ethnic origin of the study population affects the prevalence, with more case reports of antecollis originating in Japan than elsewhere.⁴⁵

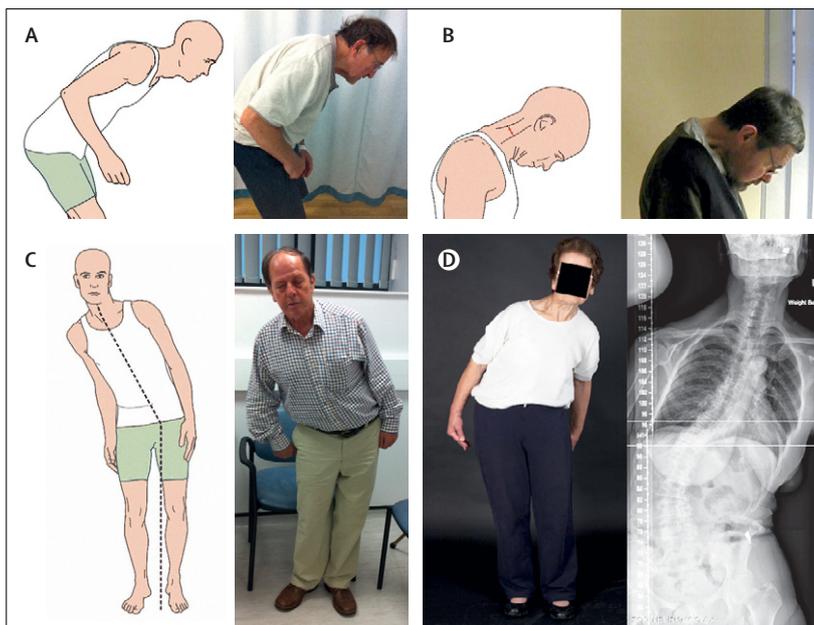


Figure 2: Sagittal plane deformities (A: camptocormia, B: antecollis) and coronal plane deformities (C: Pisa syndrome, D: scoliosis)

Clinical presentation

Antecollis can occur with a subacute onset over weeks or months.⁴⁶ It can present before the other motor features of PD,¹¹ but more usually occurs several years into the disease. Patients can complain of pain in the posterior aspect of the neck or develop problems secondary to neck flexion (difficulty swallowing, excessive drooling, or visual limitation). In the early stages, hypertrophy and active spasms might be visible in various anterior and posterior neck muscles, but after some time overstretching of posterior neck muscles and a woody feel on palpation, particularly of the splenius capitis and trapezius, become prominent.⁴² Most studies report normal strength on testing residual neck extension,^{11,42,47} and some note prominent contractions in sternocleidomastoid muscles, limiting voluntary neck extension.^{12,47} It is likely that the prevertebral deep neck flexors are also involved in antecollis development, but these are not easily assessed without invasive testing. Unlike idiopathic cervical dystonia, there is no *geste antagoniste* in PD or MSA that can improve the abnormal neck posture.⁴⁸ Antecollis in PD is often associated with substantially increased axial tone, although patients might still be capable of passive extension to the normal position. In other patients, the antecollis can become a fixed deformity, even shortly after onset (figure 2B).²³

Differential diagnosis

Investigations of antecollis should be guided by examination findings (figure 4). Antecollis is often associated with a limited range of movement as the deformity becomes more long-standing, but if there is a



Figure 3: Camptocormia in the standing, seated, and supine positions

substantial limitation of neck movement appearing subacutely or when pain is excessive, imaging is necessary to rule out cervical spine pathology. The most common alternative diagnosis to the finding of antecollis in PD is MSA, in which antecollis is frequent. Recent reports have also drawn attention to a possible role for medication-induced changes in neck posture. Antecollis might be an off-state phenomenon, or it might develop as dyskinesias appear in relation to increases in dopaminergic medications, and so fluctuations of antecollis and its relationship to medication times should be investigated. Conversely, several case reports have suggested that antecollis might be induced by dopamine agonist therapy (seven

patients received pramipexole, five cabergoline, two pergolide, and in two the drug was not specified)^{12,45,49,50} or amantadine.⁵¹ These medications should therefore be stopped on a trial basis if there is a close temporal association to the onset of the syndrome, although the antecollis is not necessarily reversible, particularly when medication is stopped late.^{49,50}

Weakness of residual neck extension should prompt a further neuromuscular work-up. Myasthenia gravis must be considered if the patient reports double vision or symptoms suggestive of fatigue. There have been occasional reports describing coincidental PD and myasthenia gravis in patients who present with antecollis.^{52,53} Weakness of neck extension can also be a presenting feature of motor neuron disease. In patients with PD with antecollis without weakness, electromyography and muscle biopsy findings can be abnormal, but are often non-specific and non-diagnostic in terms of cause or effect of the antecollis.⁴²

Treatment

Some patients with PD and MSA have reported improved head position following treatment with levodopa, but this was not a consistent finding.^{11,42,44,47,48} Muscle relaxants such as clonazepam can be helpful.¹¹ Botulinum toxin therapy is usually attempted if there are active dystonic spasms on examination, but benefit was reported in only three of 13 patients treated with injection of levator scapulae or sternocleidomastoid muscles.⁴² Botulinum toxin treatment of prevertebral deep neck flexors (longus colli and longus capitis) was beneficial in a single case but required CT guidance.⁵⁴ Other neck muscles such as the scalene and submental groups might contribute to antecollis, and the approach to each patient should be tailored according to the examination findings.

Intensive physiotherapy and the use of neck collars might be of benefit, although there is no supporting evidence.

There are few reports on management with surgical fusion⁵⁵ and DBS,¹⁰ and this should be reserved as a third-line option after oral treatment and local botulinum toxin injections.

	Country	Number of patients with PD	Prevalence (%)	Diagnostic criteria
Camptocormia				
Abe et al ⁸	Japan	153	18%	45° TL flexion
Tiple et al ⁶	Italy	275	7%	45° TL flexion
Lepoutre et al ⁹	France	700	3%	TL flexion
Ashour and Jankovic ¹	USA	164	12%	45° TL flexion
Antecollis				
Ashour and Jankovic ¹	USA	164	6%	>45° neck flexion
Yamada et al ¹⁰	Japan	126	6%	NA
Kashihara et al ¹¹	Japan	252	6%	Neck flexion
Fujimoto ¹²	Japan	131	5%	NA
Pisa syndrome				
Bonanni et al ¹³	Italy	1400	2%	>15° lateral flexion
Scoliosis				
Baik et al ¹⁴	Korea	97	33%	Radiograph (Cobb method)
Ashour and Jankovic ¹	USA	164	9%	Lateral curvature
Grimes et al ¹⁵	UK	103	60%	Clinical, radiography in 50%
Duvoisin and Marsden ¹⁶	UK	21	91%	Clinical examination
Indo and Ando ¹⁷	Japan	70	31%	Clinical examination
Serratrice and Schiano ¹⁸	France	140	13%	Clinical then radiography
Sicard ¹⁹	France	17	47%	NA
Onuaguluchi ²⁰	UK	33	15%	NA

TL=thoracolumbar. NA=data not available.

Table: Prevalence studies of postural deformity in patients with parkinsonism

Retrocollis

Retrocollis is an abnormal neck posture, with the head held in extension. It is associated with axial rigidity, and is most typically seen in patients with Richardson's syndrome (progressive supranuclear palsy; PSP) and in patients exposed to neuroleptics. It also occurs as a subtype of primary cervical dystonia.⁵⁶ Retrocollis is hardly ever seen in PD, and should therefore be regarded as a prominent red flag, in particular signalling a diagnosis of PSP.

Coronal plane deformities

Pisa syndrome and scoliosis

Pisa syndrome and scoliosis are discussed jointly here, as they share not only the plane of deformity but also the body segment involved (as opposed to camptocormia and antecollis). However, the two are clinically discernible, and also differ partly in terms of underlying mechanisms and therapeutic approach.

Definitions

Pisa syndrome refers to a marked lateral flexion of the trunk, which is typically mobile (it resolves, for example, on lying down). This postural deformity was first described as a truncal dystonia or pleurothotonus, occurring as a side-effect of antipsychotic treatment.⁵⁷ More recently, Pisa syndrome has been described in PD.⁵⁸ It has also been described in association with Alzheimer's disease treated with cholinesterase inhibitors,⁵⁹ and as an idiopathic phenomenon.⁶⁰ Pisa syndrome might be a precursor to the development of scoliosis in PD (figure 2C).

Scoliosis is defined as a lateral curve of the spine, usually combined with a rotation of the vertebrae.^{61–63} The term as used in the orthopaedic literature refers to a lateral spinal curve with specific radiological features. For this reason, we think it should not be used as a descriptive term in patients with PD with lateral trunk flexion, unless there is radiological confirmation. Many early scoliosis studies did not use radiology for the diagnosis, and probably included some Pisa syndrome cases.

There are no diagnostic criteria for Pisa syndrome, although Bonanni and colleagues¹³ proposed the following detailed definition for lateral axial dystonia: more than 15° lateral flexion of the trunk, increasing during walking, not present when supine, and in the absence of any mechanical restriction to trunk movement (ie, degenerative spinal disease), with continuous electromyographic activity in the lumbar paraspinal muscles ipsilateral to the bending side.¹³ We propose that a diagnosis of Pisa syndrome requires pronounced (at least 10°) lateral flexion, which can be alleviated completely by passive mobilisation or on lying supine. We deviated from Bonanni and colleagues' definition, because the mechanism might not be completely dystonic, and because electrophysiological studies should not be required to define a clinical

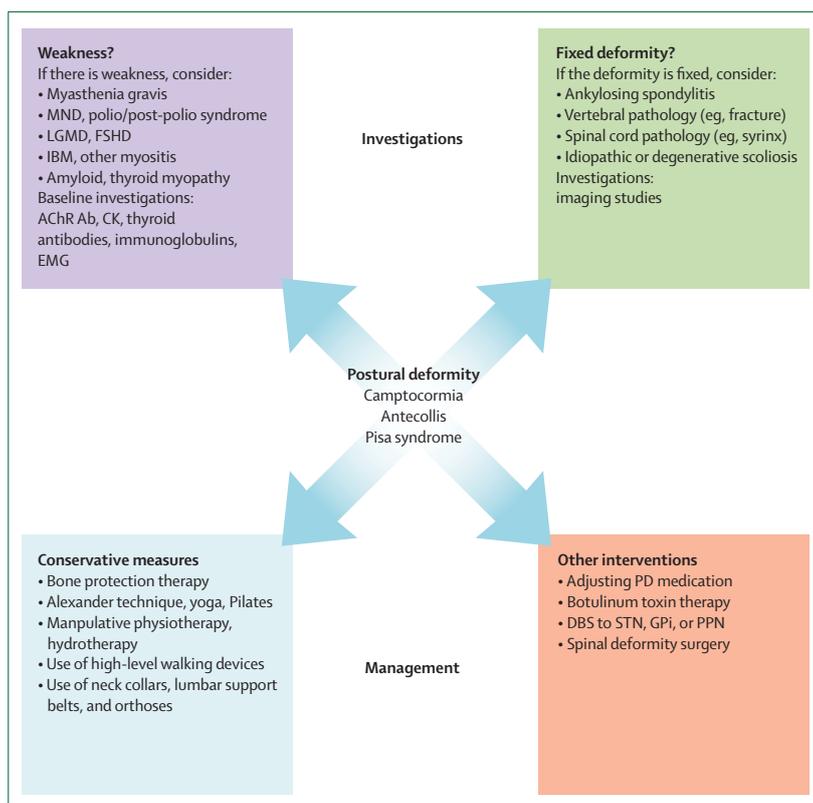


Figure 4: Differential diagnoses, investigations, and management options for postural deformity encountered in Parkinson's disease

MND=motor neuron disease. LGMD=limb girdle muscular dystrophy. FSHD=facioscapulohumeral dystrophy. IBM=inclusion body myositis. AChR=acetylcholine receptor. Ab=antibody. CK=creatinase. EMG=electromyography. DBS=deep brain stimulation. STN=subthalamic nucleus. GPi=globus pallidus interna. PPN=pedunculopontine nucleus.

syndrome. The term scoliosis should be reserved for patients whose posture cannot be improved by passive movement or supine positioning, and who have radiological evidence of a structural curve with axial vertebral rotation that persists when the effect of gravity has been eliminated (ie, on a supine image).⁶⁴

Epidemiology

A tilting to one side is very common in the later stages of PD. Scoliosis is more common in PD than in the general population, with prevalence figures ranging from 8.4 to 90.5% in parkinsonism^{14–19} and 8.5 to 60% in PD (table).^{14,15,17,18} However, these prevalence rates reflect clinical observation without radiological confirmation, and therefore might not accurately represent true scoliosis. The high variation in prevalence probably reflects the different types of parkinsonism studied (some older papers included patients with post-encephalitic parkinsonism, in which lateral flexion was often noted),⁶⁵ the variable disease duration, and the different treatments received. Similar caveats also explain the conflicting evidence about the relationship of scoliosis with disease duration and severity, treatment options, and presence of dyskinesias.^{1,15}

Clinical presentation

In the early stages most patients are not aware of any lateral flexion.¹⁶ Pisa syndrome can develop in a chronic fashion (insidious at first, with gradual worsening) or with a subacute onset followed by rapid deterioration over months.⁶⁶ It might first be noticed as the tendency of a patient to tilt to one side when sitting in a chair, with subsequent lateral flexion when they walk. When the deformity advances, patients can develop pain,^{65,67} dyspnoea, or unsteadiness leading to falls. On examination the patient will sit, stand, or walk with an involuntary lean that is consistently to one side. Patients can have impaired perception of the vertical position, and when asked to stand up straight believe they are already doing so; hence, actively moving the patient to the midline can cause them to feel unbalanced.⁶⁸

There has been debate about whether patients with lateral trunk flexion (Pisa syndrome or scoliosis) lean towards or away from their predominant parkinsonian symptom side. Most investigators found that patients tended to lean away from the most affected side,^{16,17,20,65,67} and only few authors found no association between the direction of the curve and the laterality of PD.^{14,15}

Differential diagnosis

Pisa syndrome can be diagnosed clinically on the basis of the finding of lateral flexion of the trunk, which can be corrected by passive mobilisation or supine positioning. Spinal imaging with calculation of the Cobb angle is required for diagnosing and quantifying scoliosis.⁶⁹

As with antecollis, there are reports that Pisa syndrome might be an adverse effect of medication. The archetype is that of Pisa syndrome secondary to starting dopamine-blocking agents,⁵⁷ but more recent work also points to the development of Pisa syndrome with a close temporal relationship to changes in dopaminergic medication (either the start of a new drug or a dose increase of existing medication; webvideo 3).⁷⁰ Specifically, Pisa syndrome occurred on initiation (one patient), increase (six patients), or decrease (one patient) of dopaminergic medication, and at an interval of 15 days to 3 months from medication change. Conversely, Pisa syndrome disappeared following revision of the medication change after 10 days to 3 months,⁷⁰ although like antecollis it can be irreversible. It is therefore important to review recent alterations to the patient's medication, and to note any non-dopaminergic therapies that might be contributing (neuroleptics, lithium carbonate, valproic acid, antidepressants, anti-emetics, and cholinesterase inhibitors).^{58,59,71,72}

There are two reports of Pisa syndrome developing in patients after pallidotomy, at a time interval of 4–9 years after surgery.^{73,74}

Treatment

Patients with clinical and imaging evidence of underlying myelopathy or radiculopathy should be referred for surgical intervention.³¹ Results of spinal surgery to treat

Pisa syndrome and scoliosis in patients with PD have been mixed. There are concerns that patients continue to flex laterally postoperatively,⁷⁵ and often require revision surgery.^{35,38}

Pisa syndrome (in the absence of scoliosis) in its early mobile phase might be indicative of prominent axial dyskinesia, and hence might resolve when dopaminergic therapy is modified,⁷⁰ but this is less successful in patients with long-standing postural deformities.^{66,67} Drug treatment approaches include anticholinergics and clozapine.^{13,60} Bonanni and colleagues did a blinded cross-over trial of botulinum toxin injected into the lumbar paraspinal muscles versus placebo in nine patients with Pisa syndrome; six of their nine patients experienced improvement of their posture and seven opted to continue receiving botulinum toxin treatment at the end of the study.¹³ Subthalamic DBS has been applied in ten patients with PD with Pisa syndrome, but the findings were inconclusive.⁷⁶

Spinal orthotic appliances have been tried in some patients with scoliosis or Pisa syndrome, but they are often not tolerated by patients.

Pathophysiology

The pathophysiology of axial postural abnormalities in PD is not well understood, but a number of different causes have been proposed. We begin with the evidence from animal studies for central causes then discuss the proposed central mechanisms (dystonia, rigidity, and proprioceptive disintegration). We follow with the proposals attributed to a peripheral process (myopathy, skeletal, and soft tissue changes).

Central mechanisms

Animal studies and lesioning

In the case of scoliosis and Pisa syndrome, it is likely that an asymmetrical central process has a role in the tendency to lean to one particular side. Studies in a rat model showed that chemical degeneration of an entire nigrostriatal pathway on one side produced substantial spontaneous turning ipsilateral to the lesion.⁷⁷ Similarly, hemiparkinsonism in rats (caused by injecting 6-hydroxydopamine into the left ventral tegmental area) leads to the development of substantial ipsilateral deviation and scoliosis deformity.⁷⁸ These experimental observations are consistent with clinical findings that the concavity of the scoliosis and corresponding trunk inclination are usually directed away from the clinically most affected side.¹⁶ Pisa syndrome can also occur following unilateral pallidotomy. Specifically, three patients developed Pisa syndrome to the right following left pallidotomies 4, 8, and 9 years after surgery.^{73,74} These findings support a central aetiology for initial development of coronal plane deformities, with the resulting muscle changes, tendon shortening, and contracture development being followed by degenerative bone and joint changes, eventually leading to a fixed deformity.

By contrast, the data for central lesions leading to camptocormia or antecollis are sparse, and there are no animal models of camptocormia or antecollis. Dystonic camptocormia has been reported as a complication of stroke in two patients without PD.⁷⁹ Both had vascular insults in the right putamen, but the authors do not elaborate on why patients with similar lesions do not develop camptocormia. Bloch and colleagues²² reported that camptocormic patients with PD did poorly on tests of saccadic eye movements, pointing to possible neuronal dysfunction in the midbrain. Bonneville and colleagues⁸⁰ found that camptocormic patients with PD had significantly smaller midbrain axial surface areas compared with controls, but not compared with patients with PD without camptocormia. Some believe the pedunculopontine nucleus is implicated, but the correlation seems stronger for gait freezing and postural instability than for postural deformity.²²

Dystonia

Limb dystonia is a common associated feature in young-onset PD. Flexion dystonia has been considered the cause of the characteristic stooped posture of late-stage PD, although the evidence for this is extremely limited. Support comes from the clinical observation of actively contracting muscles in certain postures (eg, early antecollis, Pisa syndrome), from anecdotal reports of patients using sensory tricks to overcome their abnormal posture,^{5,25} and from reports of improvement following botulinum toxin injection.^{5,13} Dystonia might be indicated by electromyography, and one study noted continuous paraspinal activity ipsilateral to the bending side (suggesting dystonia) in all studied Pisa syndrome cases.¹³ However, a second study found typical dystonic activity in the ipsilateral (to bending side) paravertebral muscles in only three of ten patients with PD with Pisa syndrome.⁶⁷

Most investigators feel that if a dystonic phenomenon is occurring, it probably represents an early and short-lived component of postural deformity development. This is perhaps best seen in younger patients with more mobile postural abnormalities (webvideo 1, webvideo 3). Dystonia is more often seen in patients with young-onset PD, and might be associated with genetic parkinsonism such as that linked to a Parkin mutation.^{81,82} In patients with advanced disease, this dystonic element might burn out, with secondary soft tissue, muscle, and spinal changes taking greater precedence, leading to a more fixed deformity (webvideo 2).

Impaired proprioception and kinaesthesia

Postural control is a complex system involving the integration of sensory information (vestibular, visual, and proprioceptive). Regarding the vestibular component, most studies conclude that vestibular dysfunction does not explain postural deficits in PD.⁸³⁻⁸⁶

Proprioception provides highly accurate information that helps to maintain body verticality in healthy people,⁸⁷

but studies in patients with PD have given inconsistent results. Duvoisin and Marsden¹⁶ described 19 parkinsonian patients with scoliosis (some of whom might have had Pisa syndrome), and only one of them was conscious of a tendency to lean to the side. They also reported that the scoliosis increased when patients closed their eyes, possibly indicating both defective orientation of the body in space and defective judgment of the visual vertical plane. Azulay and colleagues^{88,89} have recently supported these findings, showing that patients with PD perform poorly on tasks for which the aim is to maintain postural orientation in the vertical plane, with notable deterioration when visual input is removed. They also examined proprioceptive integration by using tendon vibration stimulation, and showed that a specific involvement of the static proprioceptive function does exist, causing a specific orientation postural deficit in PD, whereas dynamic process can be preserved or damaged later in the course of the disease.⁹⁰ Many subsequent studies have confirmed that proprioceptive function is abnormal in PD. This evidence was initially restricted to motor control of the limbs, mainly the arms.⁹¹⁻⁹⁴ Recent work has extended these findings, showing that proprioceptive defects also affect axial motor control in the yaw plane (turning about the vertical axis).^{95,96} Whether such proprioceptive defects also affect postural control in the sagittal or coronal planes requires further study, and this would have implications for understanding postural deformities such as camptocormia and Pisa syndrome.

Rigidity

Rigidity is defined as a persistent increase in muscle tone that is not velocity dependent. Froment and Gardère⁹⁷ studied changes in parkinsonian rigidity with posture, and concluded that the body has two mechanisms to protect against postural abnormalities: a maintenance stabilisation of muscular contraction (to hold the trunk erect in an unstressed state); and a reactive stabilisation of muscle activation that occurs when posture is disturbed. They suggested that the first mechanism was impaired in PD, and that the second mechanism was in constant use to maintain posture, leading to continual abnormal muscle recruitment and activation.⁹⁸ More contemporary experimental work confirms that patients with PD (not specifically with axial involvement) have a higher axial tone than controls.⁹⁹ Additionally, patients with PD respond abnormally to perturbations during stance, showing reduced intersegmental flexibility.^{100,101} Patients with PD also present with a reduced range of spinal movements, especially around the spinal axis.^{102,103} These deficits might be compensated by flexion in the sagittal or coronal planes, to maintain the centre of gravity within the limits of stability and to prevent falls. Burleigh and colleagues¹⁰⁴ studied the effect of levodopa on muscle tone in patients with PD during quiet stance. They

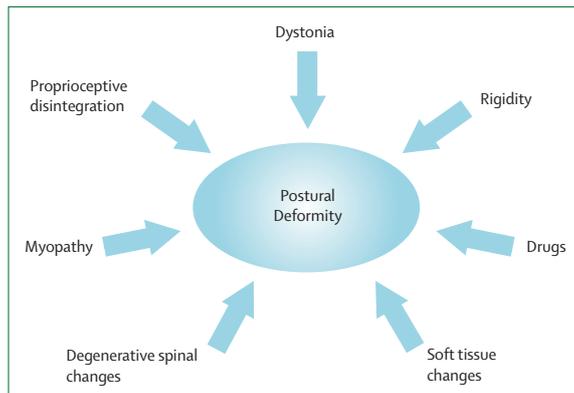


Figure 5: Possible mechanisms involved in the development of postural deformity in Parkinson's disease

found that lower extremity and trunk muscles were of high-amplitude electromyographic activity in all patients with PD when in the off state, but muscle activity was reduced when in the on state; the authors concluded that dopamine depletion results in increased muscle tone during stance, which might contribute to postural change.¹⁰⁴ Clinical and animal experiments that show a tendency to lean away from the more rigid (predominant PD symptom) side in coronal plane deformities challenge the theory that rigidity is the principal cause of postural abnormalities.^{16,18,65,67,77-78}

Drugs

There are a few reports claiming that dopamine agonists can induce or aggravate antecollis^{45,49,50} or Pisa syndrome^{70,105} in PD, with the onset of the deformity beginning between a few weeks to 18 months after treatment initiation, and usually resolving on stopping the drug. There are also reports of other medications such as cholinesterase inhibitors, valproate, and amantadine, leading to deformities, but these are single case reports or small cases series.^{51,59,71} A proposed mechanism is the imbalance between dopamine, norepinephrine, and serotonin levels, and the way in which these neurotransmitters regulate axial muscle tone.⁵⁹ Most cases have been reported from Japan, and that might reflect a genetic difference in the expression of drug-metabolising enzymes and transporters.¹⁰⁶ It is important to note that these cases are few, evidence is weak, and most patients taking dopamine agonists do not develop antecollis or Pisa syndrome.

Peripheral mechanisms

Myopathy

Evidence for myopathy has been found with electromyography (fibrillation potentials, small polyphasic motor unit potentials), muscle imaging (fatty infiltration of muscles, muscle atrophy), and muscle biopsy (abnormal histology).^{21,23,46,107,108} A concomitant specific muscle disease, such as myasthenia gravis or a focal

myositis,^{109,110} has been shown to be the cause of abnormal posture in a few cases, but it has been proposed by some that primary muscle disease could be responsible for antecollis and camptocormia in PD,^{21,23} although why patients with PD would develop such a localised myopathy is unclear. However, most studies have suggested that myopathic changes when present are non-specific and are related to disuse or denervation secondary to the severe primary postural abnormality.^{7-9,22,39,50,67,111}

Some of these discrepancies between studies might be due to the fact that electromyography of the axial musculature is technically difficult (particularly for myopathic features that require voluntary activation), normal values for these groups are unclear, superficial testing might miss out relevant deep muscles, and inter-operator reproducibility is poor.¹¹² Imaging changes in paraspinal muscles are often non-specific. Findings on muscle biopsy can reflect age-related change,¹⁰⁸ and there are few data about the histology of paraspinal muscles in patients with PD without camptocormia. Many studies failed to comment specifically on strength in the affected muscle groups.^{21,23,107,108} A recent study investigated the underlying cause of camptocormia in 63 patients (not restricted to PD).¹¹³ The results showed that 40 patients had a paraspinal myopathy, as shown by muscle weakness, CT findings (fatty infiltration restricted to the paraspinal muscles), and biopsy findings showing lobular endomysial fibrosis. The remaining 23 patients had another muscle or neurological disorder, such as limb girdle muscular dystrophy, myotonic dystrophy, or inclusion body myositis. Within the paraspinal myopathy group there were four patients with PD. Moreover, there were another four patients with PD within the group not meeting the criteria for paraspinal myopathy. This interesting study adds to growing evidence that myopathic changes can occur in PD patients with camptocormia,¹¹³ but it seems unlikely that this will prove to be the primary cause in most cases. Overall, we feel that the evidence is weighted against myopathy being a primary pathogenic mechanism.

Spinal and soft tissue changes

A history of back surgery (eg, laminectomy), trauma, or degenerative spinal conditions is common in patients with PD with postural deformities, especially in those with camptocormia.^{5-8,21,80} These factors are likely to have a direct mechanical effect on posture due to bony and soft tissue changes, and it is conceivable that they might trigger a peripherally induced (secondary) dystonic occurrence in some patients.¹³ When pain is present, it might provoke a compensatory posture, which is more comfortable and therefore becomes habitual, eventually interacting with the patient's proprioceptive sensory feedback, and thus contributing to an abnormal body scheme. Another plausible suggestion is that in the setting of chronic pain, muscle spasm develops as a protective mechanism to prevent movement about the damaged joint, thereby promoting abnormal posture.⁶⁷

In their review on striatal hand and foot deformities in PD, Ashour and colleagues² considered connective tissue changes as a potential pathophysiological mechanism in the development of deformities, particularly a loss of elasticity leading to fibrosis and atrophy, and hence fixed contracture development. It is possible that similar soft tissue changes also underlie axial postural deformities, and that the striatal hand and foot deformities occur because of the same underlying mechanisms.

Conclusions

It is essential for clinicians to keep in mind the broad differential diagnoses for postural deformities, so that potentially treatable conditions are not missed. Testing muscle power in the affected body segment is an important and often neglected aspect of the examination in postural abnormalities in PD. We list in figure 4 several conditions that might mimic or underpin various deformities. We also emphasise the need to consider the effect of prescribed medications on postural deformities.

Postural deformities are common but not inevitable in advanced PD, and the factors contributing to their occurrence need to be more clearly defined. Although for clarity we have separated the deformities into disorders of sagittal and coronal imbalance, the clinical picture is often of deformity crossing both planes. Early detection of postural abnormalities could help to avoid fixed irreversible deformities and the complications that can accompany them (pain, difficulty swallowing, shortness of breath, visual disruption, and radiculopathy).

It seems unlikely that a single pathological process can explain the differing appearances, the wide range of affected patients, and the variability of response to treatment. We propose instead that these deformities in patients with PD result from the interplay of multiple, complex factors. Important pathological changes might occur in the basal ganglia or affiliated pathways,^{22,30} and proprioceptive disintegration, loss of postural reflexes, rigidity, and dystonia are important contributory factors. Development of overt postural deformity might signal either a second hit or an additional acquired risk factor, such as degenerative spinal disease or back surgery, late-onset myopathy, acquired soft tissue changes, dystonia due to drugs, or a combination of these (figure 5). Further study is needed to determine the principal mechanisms responsible and how they interact. Priorities for future research include establishing the effect or consequence of soft-tissue changes and degenerative spinal disease in postural deformities in PD, judiciously studying any temporal relationship between use of dopaminergic medications and development of deformities, and establishing whether or not patients with postural deformity have a substandard response to levodopa compared with patients without deformity. We also suggest that large studies using botulinum toxin treatment in patients with antecollis are needed to clarify whether or not this is an effective treatment strategy, and

Panel: Proposed definitions of postural deformities in Parkinson's disease

Camptocormia

Marked (minimum 45°) flexion in the sagittal plane originating in the thoracolumbar spine, almost complete resolution in the supine position

Antecollis

Marked (minimum 45°) neck flexion (maybe partially overcome by voluntary or passive movement), unable to fully extend the neck against gravity but able to exert force against the resistance of the examiner's hand

Pisa syndrome

Marked (minimum 10°) lateral flexion that can be almost completely alleviated by passive mobilisation or supine positioning

Scoliosis

Lateral flexion not relieved by voluntary or passive movement plus lateral curvature of the spine of at least 10° as measured by the Cobb method and evidence of axial vertebral rotation on a radiograph

which muscles are best targeted. The variable prevalence of postural deformities in different countries also raises the question of whether there exists a true ethnic difference in the presentation and epidemiology of these deformities. Large comparative studies should help answer this question, and might aid our understanding of the underlying mechanisms.

To consolidate knowledge in this area, future studies would benefit from consensus diagnostic criteria for each postural deformity seen in PD. We encourage use of the criteria adopted from Ashour and Jankovic¹ for antecollis and camptocormia, and proposed by us for Pisa syndrome and scoliosis in PD (panel).

Search strategy and selection criteria

Much of the literature in this area consists of descriptive studies, such as prevalence reports, case series, or observational studies, some of which are case-control studies. Relevant studies of all types were reviewed if they added new knowledge in this area. Potential papers were identified by searching PubMed for papers published between 1966, and March, 2011, using the terms "postural abnormalities", "camptocormia", "bent spine syndrome", "Pisa syndrome", "scoliosis", "lateral flexion", "dropped head syndrome", "antecollis", "retrocollis", and "Parkinson's". Selected articles were also obtained from the reference lists of papers identified by the PubMed search, from searches of the authors' own files, and from the National Hospital for Neurology and Neurosurgery, Queen Square, London, library for historical papers.

Contributors

KMD and BRB conceived the idea for this Review. KMD, BPvdW, and BRB wrote the first draft. All authors contributed equally to subsequent drafts and editing.

Conflicts of interest

KMD has received travel expenses from Teva, Sanofi-Aventis, UCB, Ipsen, Orion, and Genus Pharmaceuticals. BPvdW has received a grant from Ipsen Pharmaceuticals and travel and accommodation expenses from Boehringer Ingelheim. LS-M has received payment for lectures from Teva and Lundbeck and travel and accommodation expenses from Genus Pharmaceuticals, Teva, and UCB Pharmaceuticals. OSG has received consultancy fees from Merck-Serono, expert testimony fees from Baker Botts, and payment for lectures from GlaxoSmithKline, Boehringer Ingelheim, and UCB. BRB has received consultancy fees from Boehringer Ingelheim, Teva, GlaxoSmithKline, and Novartis. MCP has received travel expenses from Boehringer Ingelheim, Teva, and Buxton. J-PA has received travel expenses from Boehringer Ingelheim, Abbot, and Novartis, and has received payment for lectures by Lundbeck and expert fees from Lundbeck and Novartis. All authors state that none of these travel expenses or other payments are in any way connected to the production of this paper.

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