REVIEW

Recent advancements in lateral trunk flexion in Parkinson disease

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Abstract

Purpose of review

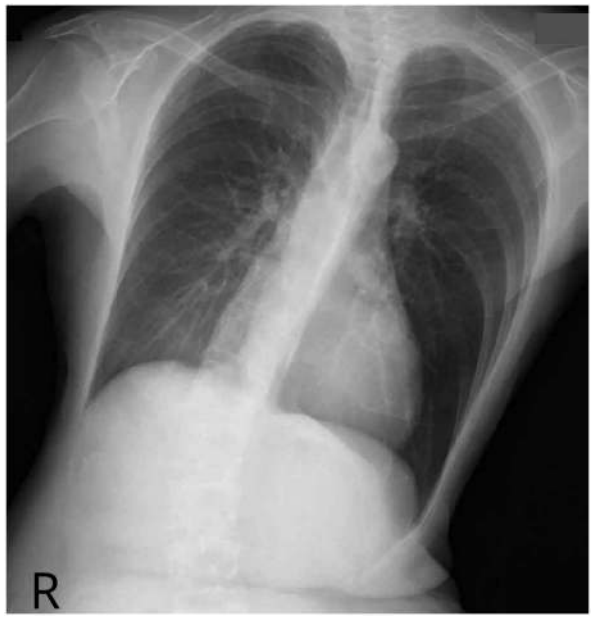
Understanding the pathophysiologic underpinnings of lateral trunk flexion (LTF) in Parkinson disease (PD) has been growing. Adjusting antiparkinsonian medications, botulinum toxin, or surgical intervention has been found efficacious in some patients. Nevertheless, these treatments remain limited, often resulting in inadequate outcomes. We review patients with LTF with PD, including recent advancements in treatment and neuroimaging examination.

Recent findings

The basal ganglia system is a major contributing factor to LTF, and the therapeutic intervention also targets the basal ganglia system, including dystonic contraction. The perceptions of the postural verticality or spatial cognition of the correct body orientation promote the severity of LTF or result in a chronic condition with irreversible structural deformities.

Conclusion

The combination of pharmacologic interventions with nonpharmacologic interventions, such as rehabilitation, might be needed to manage LTF, and the initiation of these treatments should be started as early as possible.



Lateral trunk flexion (LTF) in patients with Parkinson disease (PD) can be decreased by passive mobilization or recumbent position without mechanical restriction to the trunk movement. The feature was first defined in Pisa syndrome (PS).[1,2] Typically, patients with LTF lean toward 1 side during sitting, standing, or walking, and LTF can appear subacutely within days or weeks. The occurrence of LTF in PD is relatively rare, and a large Italian cohort comprising 1631 participants with PD estimated its prevalence to be 8.8%.[3] Often, LTF becomes irreversible, and the resulting abnormal posture affects the motor function. To date, no consensus has been attained on the definition of PS or diagnostic criteria.[1] Of late, the understanding of pathophysiologic underpinnings of LTF in PD has been growing. Thus, adjusting antiparkinsonian medications, botulinum toxin, or surgical intervention has been reported to exert efficacy in some patients with PD. Nevertheless, these treatments remain limited, often resulting in inadequate outcomes. This study aims to review LTF, including recent advancement in the treatment or neuroimaging examination.

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Multifactorial pathophysiology in PS

The pathophysiology of PS is multifactorial comprising the basal ganglia system or non–basal ganglia systems as sensorimotor dysfunction, body schema perception and cognition orientation, or the asymmetric phenomenon of trunk muscles.[1,2]

Basal ganglia system

Patients with PD exhibit a higher axial muscle tone than healthy controls,[4] and the muscle tone remarkably reduces the range of trunk movement around the axial axis.[5] Some neurophysiologic studies have reported the continuous muscle activity in the paraspinal muscles or intra-abdominal muscles ipsilateral to the bending side.[6–9] Reportedly, the lateral increased axial muscle tone was derived from dystonia.[1,2] The asymmetric phenomenon of the trunk muscle was observed on neuroimaging, detailed later.[10] Sensory tricks partially improved trunk dystonia.[1] The asymmetric increased motor tone in the trunk muscles resulting from an imbalance in basal ganglia functioning plays a primary role in the development of PS. This is supported by some animal studies documenting that axial postural deviation developed by unilateral 6-hydroxydopamine (6-OHDA) nigrostriatal lesions in rats. Moreover, the postural deviation has been reported to become more severe as the dopaminergic denervation increases.[11] Patients who had unilateral surgical lesion of the basal ganglia, such as pallidotomy, exhibited LTF contralateral to the side of the surgery.[12] Some studies reported that the exposure of dopaminergic antagonists or dopamine agonists elicits LTF.[13,14] The dopaminergic imbalance in PD creates poor symptomatic control of muscular rigidity,[15] and PD patients with PS exhibit higher motor asymmetry than those without PS.[7] LTF can occur as off-period dystonia of motor complications of PD, further supporting the major role of the basal ganglia system for LTF.[16] However, substantial asymmetric involvement of the brain stem, including basal ganglia, was not pathologically determined in a patient with PD with LTF.[17] Nonetheless, LTF was reported to be developed after the increased dosage of dopaminergic medications, the modification of which resolved LTF.[14] This finding could be indicative of axial dyskinesia. As most PS cases poorly respond to the dopaminergic treatment, other neurotransmitter systems play a role in the development of PS. Cholinesterase inhibitors elicit PS as a side effect,[2] and cholinergic nuclei are involved in regulating the axial posture tone.[18,19]

Anyway, PS is more prevalent in patients with multiple system atrophy (MSA) of parkinsonian predominance than in those with PD and has been increasingly recognized as a potential indication of MSA.[2,20] Although dystonia is recognized in MSA, axial dystonia is rarely presented.[2] Consistent with PD, axial dystonia is considered a cause of PS.[20–22] A pathologic case with right bending posture documented that neuronal loss, astrogliosis, and argyrophilic glial cytoplasmic inclusions were evident in putamen, which were much severe on the right side than on the left side.[21] Axial dystonia including PS could be associated with progressive striatal degeneration in MSA.

The postural orientation and postural stabilization are controlled by the proprioception, vision, and vestibular system, which are impaired in PD.

Associated systems with the basal ganglia system

Studies have indicated a deficit in spatial cognition of the correct body orientation about gravity or impairment in the integration of information from visual, vestibular, or somesthetic sources as a critical factor in the pathophysiology of PS.[1,23] The postural orientation and postural stabilization are controlled by the proprioception, vision, and vestibular systems, which are impaired in PD.[23,24] After a unilateral thalamotomy, transient contralateral trunk flexion associated with vestibular dysfunction was evident in patients with PD.[25] In addition, peripheral unilateral vestibular hypofunction, probably elicited by the damage of vestibular pathways, was observed in patients with PD with PS.[26] Patients with PD with PS experience the subjective visual vertical deviation compared with healthy controls, and the deviation could be partially related to a deficit in the vestibular function.[27] The perception of the postural verticality in PD is indicated by an alteration in vestibular or proprioceptive integration resulting from basal ganglia disorders.[28] Furthermore, executive function or attentional impairment is reported more in PD with PS.[29,30] However, whether such impairment is the cause or the result of the postural deviation remains unclear.

Peripheral systems

An alteration in the musculoskeletal muscle, such as myopathy or soft-tissue changes, can accelerate abnormal postures[1,2]; these changes might be tardive and resistant to levodopa. Most

Figure 1 CT of the unilateral lumbar quadrate muscle (psoas major muscle) in a patient with lateral trunk flexion

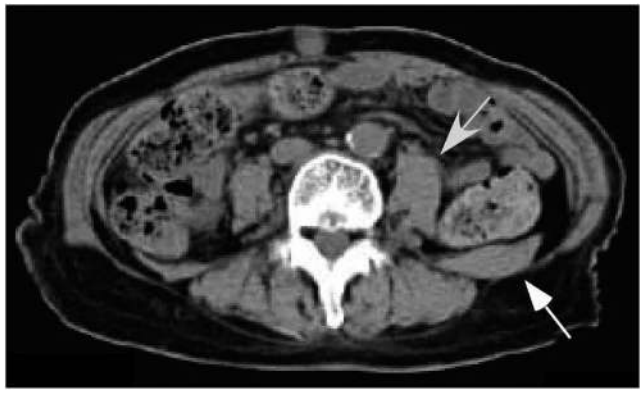


Table 1 Neuroimaging of intra- and extra-abdominal muscles in Parkinson disease with LTF

					Hypertrophy side			Side on which hypertrophy was marked				
	Sex	Disease duration (y)	PD affected side	Bending side	Lumbar quadrate muscle	Psoas major muscle	Abdominal oblique muscles	Paraspinal muscles	Multifidus muscle	Latissimus dorsi	Iliopsoas	Spinal level
Patient 1 [10]	F	6	R	R	L	L	R	L[a]				L4, CT
Patient 2 [10]	M	8.2	L	R	L	L	L	L[a]				L4, CT
Patient 3 [10]	F	6.4	L	R	R	R	R	R[a]				L4, CT
Patient 4 [10]	F	18	R	R	R	R	R	R[a]				L4, CT
Patient 5 [10]	F	0.8	L	L	R	R	R	None[a]				L4, CT
Patient 6 [10]	F	5.5	R	R	L	L	L	L[a]				L4, CT
Patient 7 [10]	F	3.5	L	R	R	L	R	L[a]				L4, CT
Patient 8 [10]	M	1	L	L	R	R	R	R[a]				L4, CT
Patient 9 [7]	M	11	L	L					L	L	L	Lumbar position, CT
Patient 10 [7]	M	9	L	L					L	L	L	Lumbar position, CT
Patient 11 [7]	M	8	L	L					L	L	L	Lumbar position, CT
Patient 12 [7]	M	13	L	L					L	L	L	Lumbar position, CT
Patient 13 [7]	M	14	L	L					L	L	L	Lumbar position, CT
Patient 14 [7]	M	17	L	L					L	L	R	Lumbar position, CT
Patient 15 [7]	M	7	L	L					R	R	R	Lumbar position, CT
Patient 16 [7]	M	4	L	L					R	R	R	Lumbar position, CT
Patient 17 [7]	M	15	R	R					L	L	L	Lumbar position, CT
Patient 18 [7]	M	7	R	R					L	L	L	Lumbar position, CT
Patient 19 [7]	M	9	L	L					None	None	None	Lumbar position, CT
Patient 20 [7]	M	9	L	L					R	R	None	Lumbar position, CT
Patient 21 [7]	M	12	L	L					R	R	R	Lumbar position, CT
Patient 22 [7]	M	8	L	L					None	None	None	Lumbar position, CT
Patient 23 [7]	F	12	L	L					None	None	None	Lumbar position, CT
Patient 24 [7]	F	11	R	R					L	L	L	Lumbar position, CT

Continued

Table 1 Neuroimaging of intra- and extra-abdominal muscles in Parkinson disease with LTF *(continued)*

					Hypertrophy side			Side on which hypertrophy was marked				
	Sex	Disease duration (y)	PD affected side	Bending side	Lumbar quadrate muscle	Psoas major muscle	Abdominal oblique muscles	Paraspinal muscles	Multifidus muscle	Latissimus dorsi	Iliopsoas	Spinal level
Patient 25[7]	F	6	R	R					L	L	L	Lumbar position, CT
Patient 26[7]	F	8	L	L					NA	R	L	Lumbar position, CT
Patient 27[7]	M	11	R	R					L	L	R	Lumbar position, CT
Patient 28[7]	F	7	R	R					L	L	L	Lumbar position, CT
Patient 29[6]	F	12	L	R				R				L1 to S1, MRI
Patient 30[6]	M	7	L	R				L				L1 to S1, MRI
Patient 31[6]	F	13	R	R				R				L1 to S1, MRI
Patient 32[6]	M	12	Bilateral	R				R				L1 to S1, MRI
Patient 33[6]	M	10	R	R				None				L1 to S1, MRI
Patient 34[6]	F	2	L	R				NA				L1 to S1, MRI
Patient 35[6]	F	10	L	R				L				L1 to S1, MRI
Patient 36[6]	F	9	Bilateral	R				L				L1 to S1, MRI
Patient 37[6]	F	6	L	R				None				L1 to S1, MRI
Patient 38[6]	F	9	R	L				R				L1 to S1, MRI
Patient 39[6]	F	13	Bilateral	L				R				L1 to S1, MRI
Patient 40[6]	M	7	L	L				R				L1 to S1, MRI
Patient 41[6]	M	9	L	L				R				L1 to S1, MRI

LTF = lateral trunk flexion; PD = Parkinson disease.
[a] Hypotorphy.
The highlight shows hypertrophy ipsilateral to the bending side and this finding suggests the dystonic contractions.

myopathic changes have been suggested to be nonspecific and associated with disuse or denervation secondary to postural abnormality. A history of back surgery, trauma, or degenerative spinal conditions and related medical conditions (osteoporosis or arthrosis) increase the risk of PS.[3] In addition, compensatory postures to temporarily relieve back pain might adversely affect the proprioceptive and vestibular systems in the long term, resulting in the development of an abnormal body scheme.[2] These concomitant factors potentially accelerate postural deformities, and the long-standing axial skeletal deformities produce irreversibility of LTF.

Role of neurophysiology

In a large cohort study, the ratio of contralateral or ipsilateral of the trunk deviation was nearly 1:1.[3] EMG has revealed hyperactivity in the ipsilateral muscles to the bending side in patients with PD with LTF. The hyperactivity was observed not only in ipsilateral but also contralateral muscles.[6–8] Di Matteo et al.[8] reported that the dystonic contraction in the thoracic-lumbar paraspinal muscles was ipsilateral to the bending side. The EMG activity of the lumbar paraspinal muscles ipsilateral to the bending side was elevated during

standing or walking. Tizzani et al.[6] reported 2 patterns of hyperactivity; the lumbar paraspinal muscles contralateral to the bending side exhibited hyperactivity, and a compensatory mechanism for the trunk deviation possibly contributed to the hyperactivity of contralateral paraspinal muscles. Another pattern was characterized by the hyperactivity of the paraspinal muscles ipsilateral to the leaning side. In addition, such hyperactivity was observed in non–paraspinal muscles such as external oblique and rectus femoris muscles.[6] Regarding the intra-abdominal muscles, 1 patient with PD with PS exhibited continuous hyperactivity on EMG in the lumbar quadrate muscle ipsilateral to the bending side.[31] Notably, the hyperactivity ipsilateral to the bending side of extra- and intra-abdominal muscles is dystonic.

Role of neuroimaging

Hypertrophy ipsilateral to the leaning side

A lumbar quadrate muscle plays a role in both bending forward and leaning the lateral trunk, and a psoas major muscle contributes to bending the pelvis; these muscles increase in volume on CT (figure 1 and table 1).[10] Previous studies have interpreted the hypertrophy ipsilateral to the bending side in LTF as possibly dystonic.[6–8,10] A patient with PD with PS exhibited continuous hyperactivity on EMG in the lumbar quadrate muscle ipsilateral to the bending side,[31] signifying a dystonic contraction. The dystonic hypertrophy of not only paraspinal but also non–paraspinal muscles might play a role in determining the ipsilateral lateral bending; however, it is marginally observed in the internal and external abdominal oblique muscle.[10] Such unilateral hypertrophy ipsilateral to the bending side is likely to be evident in patients with rapid-onset LTF.[10] Moreover, the hypertrophy is often reported in the paraspinal muscles ipsilateral or contralateral to the leaning side as palpable contractions[6,7,10] (figure 2). A study reported that the hypertrophy ipsilateral to the leaning side was slightly frequent at the levels of L2 and Th11 and possibly occurred in the very early phase of LTF.[10] EMG in the supine position revealed abnormal tonic hyperactivity in the paraspinal muscles and abdominal external oblique muscles ipsilateral to the leaning side.[6–8] Furthermore, the hypertrophy of the paraspinal muscles ipsilateral to the bending side is considered dystonic.[10] Although the unilateral hypertrophy in the paraspinal muscles contralateral to the leaning side has also been reported, this finding intensified from L4 to Th10.[10] This increase in the muscle size might result from the compensatory mechanism of attempting to straighten the trunk.

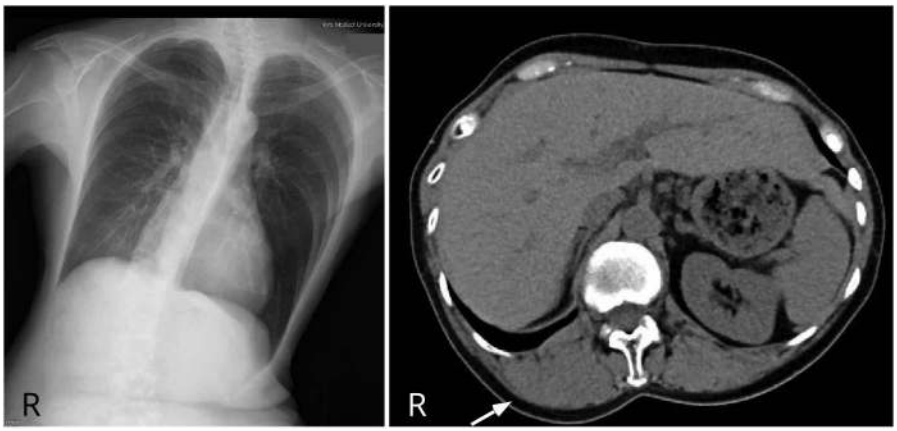
Hypotrophy contralateral to the leaning side

The hypotrophy of the lumbar quadrate muscle, psoas major muscle, or internal abdominal muscles ipsilateral to the bending side is evident.[10] Perhaps the hypotrophy results from secondary mechanisms to muscle disuse, and such patients have the hypotrophy of the paraspinal muscles or the external abdominal muscles ipsilateral to the bending side.[10] Fatty changes on MRI are frequently observed in such atrophic muscles.[7] The hypotrophy can accelerate the trunk bending and is frequent in patients with longer durations of LTF (table 1). PD rarely has double LTF.[32] In a study, a patient with left-sided LTF subsequently presented with right-sided LTF.[32] At the onset of right-sided LTF, the left lumbar quadrate muscle was found to have increased in volume on CT (figure 3); this change was slightly evident in the psoas major muscle and marginally observed in other extra-abdominal muscles. The hypotrophy ipsilateral to the bending side is not a target for the treatment for LTF such as botulinum toxin. Furthermore, hypotrophy or atrophy contralateral to the bending side could be caused by secondary mechanisms because of stretching stress on the muscles.

Other roles

The classification of primary or secondary axial myopathy in patients with LTF, particularly in those with long-lasting LTF, could be challenging. Regarding camptocormia in PD, the duration corresponds with radiologic muscle findings.[33]

Figure 2 X-ray and CT of the unilateral paraspinal muscles in a patient with lateral trunk flexion



A clinical clue to differentiate scoliosis and LTF is that scoliosis does not resolve in the lying position.

Edema and swelling in the paravertebral or intra-abdominal muscles are identified as acute changes up to 31 months of the disease duration, whereas fatty degeneration is characterized as a chronic change.[34] Muscle biopsy in the paraspinal muscles revealed active myositis. However, either primary or secondary myopathy occurs in both the acute and chronic phase. In patients with LTF, the hypertrophy on CT and the constant hyperactivity on EMG of the intra-abdominal or paraspinal muscles ipsilateral to the bending side are interpreted as dystonic,[10,32] and these findings suggest primary myopathy from neurodegenerative diseases. The atrophy with fatty degeneration can be observed in both sides and could be caused by secondary mechanisms because of stretching stress or disuse on the muscle.[1]

A clinical clue to differentiate scoliosis and LTF is that scoliosis does not resolve in the lying position. Clinicians should be in mind the possible coexistence of scoliosis with PS. A radiograph at standing and supine positions could be useful to eliminate structural bone changes, scoliosis, or the vertebral rotation. Spinal imaging could be used to calculate the Cobb angle or finding myelopathy or radiculopathy derived from LTF.

Management of LTF

Pharmacies

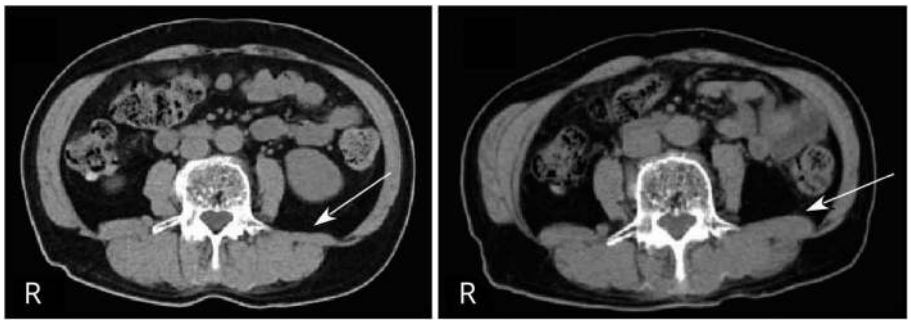
LTF can subacutely develop after any type of medication change or an increase/decrease in dopaminergic medications, especially in dopamine agonists. Most cases with LTF exhibit little response to the modification of PD medications. Previously, reversible PS in response to an antiparkinsonian drug has been reported only in 16 patients (table 2).[17,35–38] The disease duration ranged from 3–10 years. In several patients, the removal or decline of antiparkinsonian drugs successfully resolved LTF; the suspension of rasagiline, pergolide, or pramipexole, or the dosage reduction of pergolide or levodopa. Switching to another dopamine agonist, switching from levodopa/carbidopa/entacapone to levodopa/benserazide, or switching from levodopa/carbidopa/entacapone to levodopa/benserazide, eliminated LTF in each patient. Many LTF resolved within 1–4 months, and LTF shortly disappeared in 3 patients. In 1 patient, LTF was resolved by an increase in levodopa,[38] indicating that LTF could be a motor complication of PD.[13] Perhaps, the pharmacologic intervention might be effective in LTF with subacute onset, if it was started shortly after the onset of LTF, but ineffective in chronic form of LTF. Drug-induced PS appears after the introduction of antipsychotics, mood stabilizers, antidepressants, or cholinesterase inhibitors. Although the pharmacologic therapy for drug-induced PS has not been established, this condition commonly resolves after the suspension of or reduction in daily doses of these drugs.[1] Reportedly, anticholinergic drugs are effective in approximately 40% of patients.[39]

Botulinum toxin

Botulinum toxin injection into the obliquus abdominis muscle, rectus abdominis muscle, iliopsoas, or paraspinal muscles is useful for posture abnormality, including LTF.[9,40] In patients with PD with LTF, a blinded crossover study reported the efficacy of the botulinum toxin injection into the paraspinal muscles ipsilateral to the bending side in 6 of 9 patients who failed to experience the benefit from oral medications.[9] In 4 regularly treated patients, the trunk deviation was less pronounced 1/2 years after the botulinum toxin injection compared with baseline. The effective duration of the botulinum toxin was reported to be > 3 months.

Reportedly, the botulinum toxin injection in the lumbar quadrate muscle ipsilateral to the bending side entirely resolved LTF, and the effect persisted for 1 year.[31] In this patient, the lumbar quadrate muscle exhibited continuous hyperactivity on EMG. The unilateral hypertrophy ipsilateral to the bending side on CT scans could be useful in determining the target of

Figure 3 Left-and right-sided lateral trunk flexion (LTF) in a patient who had recurrent and alternating LTF



Left, at left-sided LTF, the first CT at the L4 vertebral level revealed that the area of the left psoas major muscle was smaller than that of the right psoas major muscle (white arrow). Right, after the left-sided trunk flexion was changed to the right-sided, the area of the left psoas major muscle increased (white arrow).

Table 2 Parkinson disease with reversible LTF by modifying anti-parkinsonian medications

Age/sex	Disease duration (y)	LTF direction	Involved side at LTF onset	Priming drug	Duration from priming drug to onset of LTF	LTF cessation latency	Therapy for LTF
64/M[31]	5	R	L	Rasagiline addition	3 wk	4 wk	Rasagiline withdrawn
73/M[31]	5	L	L	Rasagiline addition	4 wk	4 wk	Rasagiline withdrawn
72/M[31]	7	R	L	Rasagiline addition	3 wk	2 wk	Rasagiline withdrawn
67/F[31]	5	R	L	Rasagiline addition	4 wk	3 wk	Rasagiline withdrawn
56/M[32]	3	R	NA	Pergolide addition	4 mo	3 mo	Switched to another dopamine agonist
62/M[33]	8	L	L[a]	Switching of levodopa/benserazide to levodopa/carbidopa/entacapone	2 wk	Few days	Switched from levodopa/carbidopa/entacapone to levodopa/benserazide (600/150 mg/d)
62/M[34]	9	R	NA	Switching of levodopa/benserazide to levodopa/carbidopa/entacapone	1 mo	10 d	Switched from levodopa/carbidopa/entacapone to levodopa/benserazide (200/50 mg/d)
62/M[34]	5	R	NA	Pergolide increase	2 mo	3 mo	Pergolide reduction (1.5 mg)
68/M[34]	9	R	NA	Pergolide increase	2 mo	3 mo	Pergolide reduction (1 mg)
51/M[34]	3	L	NA	Pergolide increase	3 mo	3 mo	Pergolide suspension
57/F[34]	8	R	NA	Pramipexole increase	2 mo	40 d	Pramipexole suspension
60/M[34]	8	R	NA	Levodopa increase	2 mo	2 mo	Levodopa reduction (200 mg)
73/F[34]	7	L	NA	Levodopa increase	15 d	20 d	Levodopa reduction (100 mg)
62/M[34]	7	L	NA	Pergolide suspension	2 mo	1 mo	Levodopa increase (1100 mg)
76/M[35]	10	R	L[a]	NA	NA	3 mo	Levodopa increase (1200 mg)
64/F[35]	7	L	L[a]	NA	NA	3 mo	Levodopa increase (900 mg)

Abbreviations: LTF = lateral trunk flexion; NA = not available.
[a] At PD onset.

the botulinum toxin treatment.[10] However, clinicians should be aware that the lumbar quadrate muscle or the psoas major muscle exhibits 2 hypertrophic patterns, and the hypotrophy ipsilateral to the bending side is not the target for the botulinum toxin injection.[10] Determining the target site in the lumbar quadrate muscle for the injection of botulinum toxin could be difficult. In a patient with PS, needle EMG was used for the detection of the target in the lumbar quadrate muscle.[31] The combination of CT or MRI with needle EMG can ascertain the target site of the lumbar quadrate muscle.

Rehabilitation

Some rehabilitation studies in patients with PD with PS reported a decline in lateral bending. The reported rehabilitation programs were heterogeneous, and stretching exercises were included in all studies.[1] Only 2 studies were found to investigate the rehabilitation program specialized for LTF comprehensively without another intervention such as botulinum toxin. Previously, a patient, in whom PS persisted for >1 year, recovered after the rehabilitation alone on the stable doses of antiparkinsonian drugs.[14] The angle of LTF decreased from 27° to 4°. Although asymmetric unilateral hypertrophy of the abdominal external oblique muscles was unchanged on CT, in paraspinal muscles, it was reduced. In brief, of the rehabilitation programs, physical rehabilitation was performed for 2 weeks. Physical therapy comprised "bridge" exercises and straight leg raising in the supine position, as well as stretching exercises of both hips, knees and ankle joints, and the trunk muscles. Furthermore, five-steps balance exercises and 6-steps resistance-training exercises were performed.

Surgical intervention

Few studies have reported the surgical interventions for PS in PD. The subthalamic nucleus deep brain stimulation (DBS) reported a substantial improvement in patients with mild-to-moderate PS at a 6-month follow-up.[2,41] Ricciardi et al.[42] reported that unilateral pedunculopontine stimulation offers short-term benefits in PS. However, PS occurred after basal ganglia surgery.[2,12,43] Spinal surgery for complex spinal deformities might be challenging, regardless of conservative management. The benefit evidence sufficient for its selection

is not available because of occurring complications or frequent need for revision surgery.

Repetitive trans-spinal magnetic stimulation revealed an immediate beneficial effect on camptocormia in patients with PD.[44] Galvanic vestibular stimulation exerts a substantial effect on the subject's posture or standing balance by activation of vestibular afferents.[45] Galvanic vestibular stimulation mild to moderately improved the anterior bending posture in patients with PD, irrespective of the duration, severity of the disease, or postural deformities, and galvanic vestibular stimulation decreased the postural instability and/or abnormal axial posture.[46,47] As the effect of these stimulations' approach no longer persisted, recurrent treatments might potentially induce longer term improvement.

Overlaps with camptocormia

Patients with PD with LTF generally exhibit a combination with anterior trunk flexion, and both LTF and forward flexion are associated with PS. Anterior trunk flexion, the so-called "camptocormia," is marked by severe involuntary flexion of the thoracolumbar spine while walking, walking or sitting, but it disappears completely in the recumbent position. Camptocormia is increasingly recognized as a feature of parkinsonian disorders and related to multiple neurologic, spinal, and neuromuscular etiologies.[48] Muscle diseases involving the axial muscles, such as focal myositis or secondary myopathies, are primary causes of camptocormia.[34] Secondary muscle diseases are associated with not only neurodegenerative diseases but also an injury in the setting of kyphotic postural changes and the age-dependent loss of tissue elasticity. Axial rigidity or dystonia of the flexion muscles with weakness of the erector spinal muscles plays a role in the pathogenesis of parkinsonian camptocormia.[34] Most patients with camptocormia have a combination of rigidity and dystonia in the rectus abdominus, and the botulinum toxin injection into the muscle decreases the severity of camptocormia.[49,50] Further support for the dystonic mechanism is offered by our study documenting that hypertrophy of the rectus abdominis on CT was evident in patients with PD who had palpable abdominal muscle contractions probably contributing to the development of a stooped posture.[51] Several clinical aspects (negative EMG results, negative sensory trick testing, and lack of positive effects of the botulinum toxin treatment) argue against this assumption. Camptocormia can be a rare pharmacologic side effect of dopaminergic agonists, antipsychotics, antiepileptics, and cholinesterase inhibitors/anticholinergics.[34,48] Initially, LTF with a clinical overlap of camptocormia was assumed to be induced by antipsychotic drugs.[34] In PD, camptocormia is characterized by mild-to-moderate low back pain, which can accelerate the severity of camptocormia. Camptocormia is accepted as a levodopa-unresponsive axial symptom.[52] In such patients, camptocormia was suggested to be caused by nondopaminergic mechanisms such as myopathy. Long-lasting ATF contributes to lower responsiveness to levodopa. Approximately 20% of patients with PD with camptocormia responded to oral levodopa, and this observation was associated with dopa-responsive axial dystonia[53] or flexion dystonia of the trunk.[52] More recently, 2 phenotypes of levodopa responsiveness existed in patients with abnormal posture. The phenotypes of levodopa responsiveness with abnormal posture are associated with an "off" state, particularly in patients with ATF rather than those with LTF or PS.[54] Levodopa medication should be tried in such patients. However, the therapeutic efficacy of antiparkinsonian medications for camptocormia seems to be limited. Reportedly, the botulinum toxin injection into the rectus abdominis, DBS, or a backpack using a "sensory trick" can improve camptocormia[34,48,55]; the efficacy of these treatments, particularly LTF with an overlap of PS, might not be long lasting.

Limitations

This study has some limitations. First, we searched review articles, articles, and case reports published in English in PubMed using the following keywords: lateral trunk flexion, PS, camptocormia, Parkinson, parkinsonism, and multiple systemic atrophy. As publications, particularly in previous review articles, were relevant for this review, this review might not contain some observations provided by articles or case reports.

Conclusions

The basal ganglia system is a major contributing factor to LTF, and the therapeutic intervention also targets the basal ganglia system, including dystonic contraction ipsilateral to the leaning side. The dystonic contraction represents an early phase from the onset of LTF. The perceptions of postural verticality or spatial cognition of the correct body orientation promote the severity of LTF or result in a chronic condition with irreversible structural deformities. As patients with PD with PS exhibited a markedly prolonged disease duration or more severe disease,[3] these treatments should be initiated as early as possible. The combination of pharmacologic and nonpharmacologic interventions, such as rehabilitation, might be needed to manage LTF. Several areas of expertise, such as neurologists, physiatrists, psychiatrists, orthopedic surgeons, or rehabilitation, could make a comprehensive strategy to address PS.

Author contributions

H. Kataoka: drafting/revising the manuscript, data acquisition, study concept or design, and analysis or interpretation of data. K. Sugie: drafting/revising the manuscript.

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TAKE-HOME POINTS

- The pathophysiology of PS is multifactorial comprising the basal ganglia system or non–basal ganglia systems
- The basal ganglia system is a major contributing factor to LTF.
- The therapeutic intervention targets the basal ganglia system, including dystonic contraction ipsilateral to the leaning side.
- The intra-abdominal muscles in LTF exhibit 2 hypertrophic patterns, with the hypertrophy ipsilateral to the bending side as the target.
- The combination of pharmacologic interventions with nonpharmacologic interventions by several areas of expertise is warranted to manage LTF.

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