Chapter 4
Extrapyramidal Disorders

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4.1 Neuroanatomy and Neurophysiology

The portions of the brain and brainstem that are not a part of the direct corticopyramidal system contributing to motor control are collectively known as the extrapyramidal system. The system includes neural pathways through basal ganglia, reticular formation of the brainstem, vestibular nuclei, and red nuclei. Though the basal ganglia and their associated diencephalic and mesencephalic structures have been traditionally referred to as the extrapyramidal system, it is difficult to ascribe specific neurophysiological functions to these diverse groups of motor control areas and for the same reason, the use of "extrapyramidal" is beginning to fade, both clinically as well as neurophysiologically.

The basal ganglia and its related nuclei primarily engage in motor control and have certain roles in motor learning, behavior, emotions, and executive functions. Anatomical and functional components of the basal ganglia differ in each literature. The corpus striatum, amygdala, and claustrum are the three anatomical components of the basal ganglia. The corpus striatum is the largest structure present in the basal ganglia and because of its functional association, literature considers substantia nigra, subthalamic nucleus, red nucleus, and reticular formation as the physiological parts of the basal ganglia.

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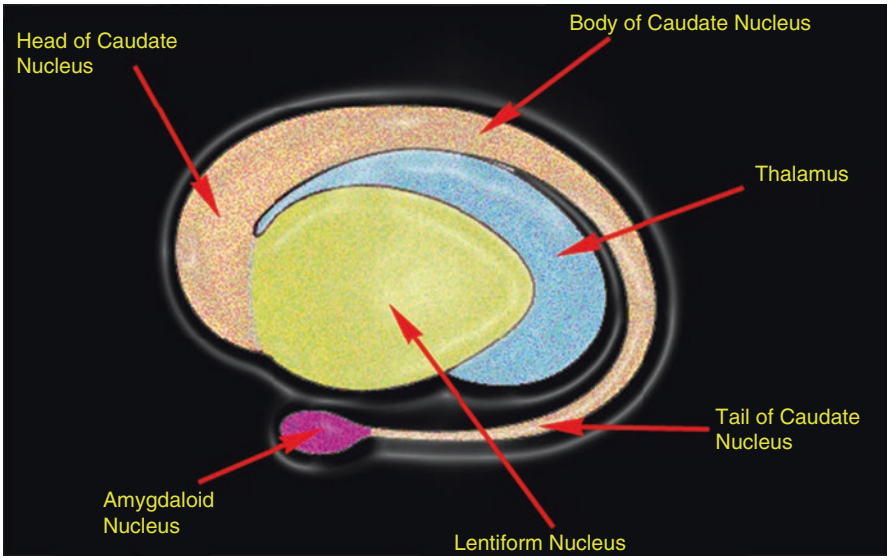

Fig. 4.1 An illustration of the anatomical structure, the corpus striatum

Anatomically, the corpus striatum is made up of two structures: caudate nucleus and lentiform nucleus (Fig. 4.1). The caudate nucleus, the "C"-shaped part of basal ganglia that lies lateral to the thalamus, closely related to the lateral ventricle, has a wide head (caput) anteriorly, a tapered body (corpus) posteriorly, and a tail curled forwardly. Located lateral to the caudate nucleus and thalamus and deeply buried within the white matter of each cerebral hemisphere is a lens or wedge-shaped subcortical structure called the lentiform nucleus. The lentiform nucleus is comprised of the globus pallidus (pallidum) medially and the putamen laterally. The anterior limb of the internal capsule partially separates the caudate nucleus from the putamen of the lentiform nucleus (Fig. 4.2). The globus pallidus, phylogenetically an older structure, is somewhat pale in appearance owing to the presence of myelinated fibers. The pallidum is further divided into globus pallidus interna medially and globus pallidus externa laterally, by a medial medullary lamina.

Situated in the temporal lobe, close to the uncus, a small oval or almond-shaped structure, closely related to the hypothalamus, the hippocampus, and the cingulate gyrus is the amygdaloid nucleus. Being a part of the olfactory and limbic systems, the nucleus plays an essential role in the sense of smell, motivation, and emotional behavior. The claustrum, the third anatomical component of basal ganglia, is located between the insular cortex and the putamen. Though the claustrum has extensive connections with many regions of the cerebral cortex, its functions are largely mysterious and may play a certain role in synchronizing different perceptual, cognitive, and motor functions.

Functionally, the basal ganglia have an afferent and an efferent region. The caudate nucleus and the putamen, together known as the "striatum," considered to be

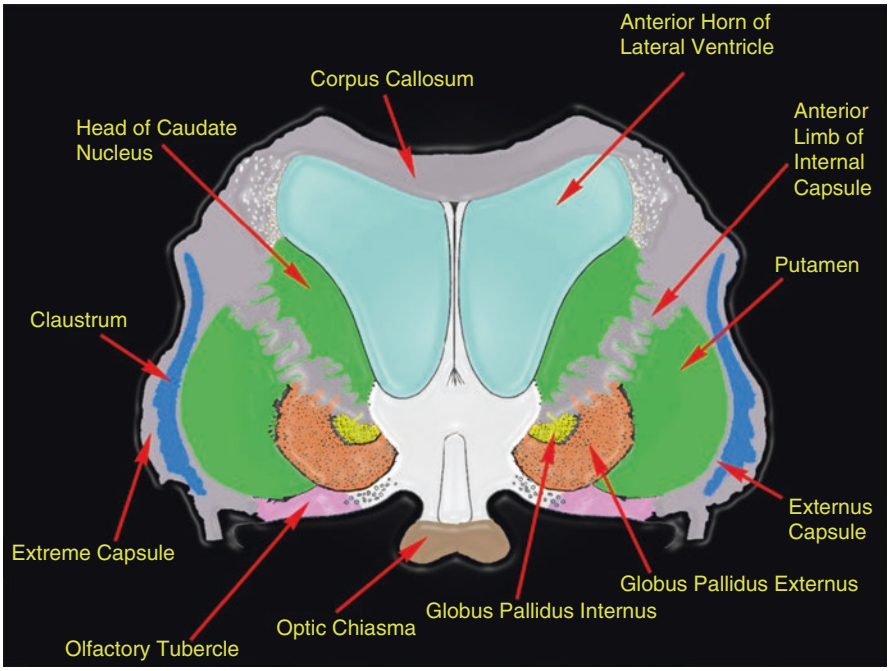

Fig. 4.2 The coronal section of the basal ganglia, demonstrating the partial separation of the caudate nucleus from the putamen by the anterior limb of the internal capsule

the input center or region of basal ganglia, receive input from most parts of the cerebral cortex (corticostriate fibers), the intralaminar thalamic nuclei, the substantia nigra, and the dorsal raphe nucleus (Fig. 4.3). The corticostriate fibers from each region of the cortex project to a specific part of the striatum. Most of the striatal inputs for the caudate region originate from the association cortex and most of the striatal inputs for the putamen region originate from the sensorimotor cortex. The extensive somatotopically arranged projections from the cerebral cortex, predominantly from the ipsilateral sensorimotor cortex, suggest a close inter-functional relationship between the striatum and the cortex. The projections from the thalamus are also somatotopic and predominantly originate from the centromedian nucleus, a part of the intralaminar nucleus of the thalamus.

Information received from the different regions of the brain is processed in the striatum and then sent to the globus pallidus and the substantia nigra, the functional output or efferent regions of the basal ganglia (Fig. 4.4). Information from these structures are transmitted to the ventroanterior and ventrolateral nuclei of the thalamus via the pallidothalamic tracts and then to the cortex. In addition to the above, the pallidal and nigral outputs also project to the superior colliculus and the reticular formation of the brainstem. Like the cerebellum, the basal ganglia have no direct descending pathway to the alpha or gamma motor neurons of the spinal cord.

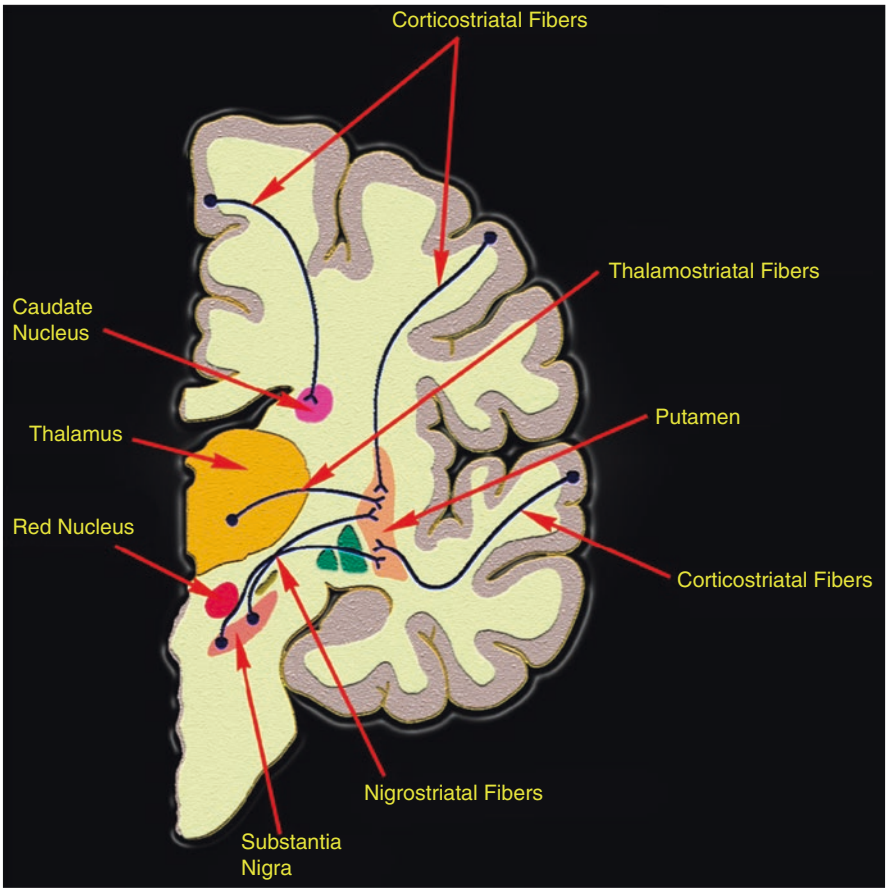

Fig. 4.3 A pictorial illustration of the afferent connections of the basal ganglia

However, the ganglia can influence the motor system through its thalamic and subthalamic projections, and its projections to the brainstem networks, together with those via the thalamocortical loops, contribute to the control of postural muscle tone and locomotion.

Except for the corticospinal pathway (pyramidal tract) arising from the cerebral cortex, four out of five crucial descending tracts from the brain arise from the brainstem and constitute the extrapyramidal tracts. The medial and lateral reticulospinal tracts are largely uncrossed and terminate on the interneurons located at the spinal cord and mainly influence the axial and proximal muscles of the extremities and are primarily responsible for locomotion and postural control. The vestibulospinal tract fibers that primarily arise from the medial and lateral vestibular nuclei are largely uncrossed and terminate on the interneurons and are responsible for extensor muscle activity and postural control. The rubrospinal tract fibers arising from the red

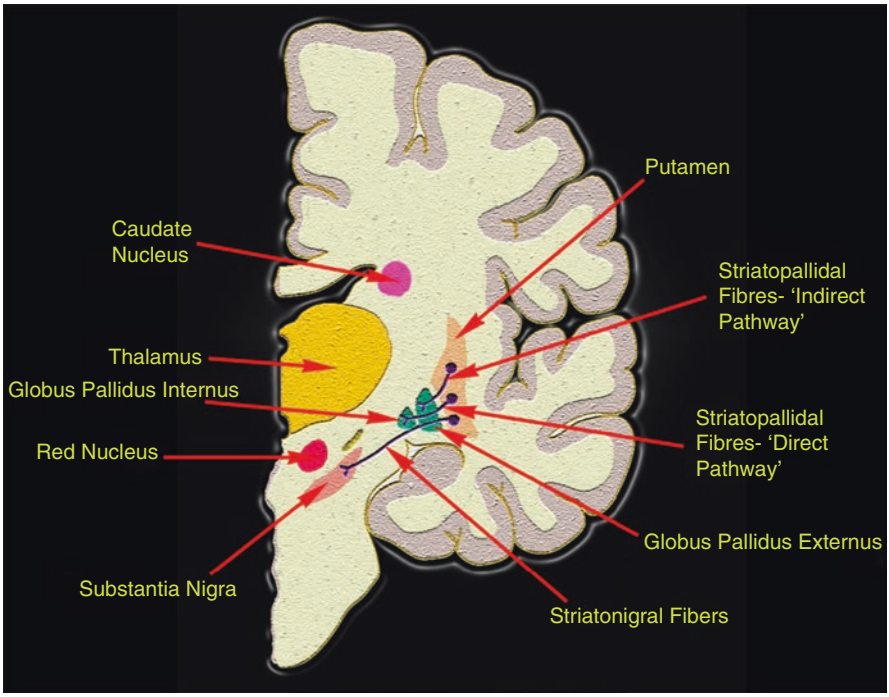

Fig. 4.4 A pictorial illustration of the efferent connections of the basal ganglia

nucleus are crossed and mostly terminate on interneurons in the cervical cord. These fibers are believed to control muscle tone and have an excitatory effect on the flexor muscles and an inhibitory effect on the extensor muscles. Projections from the globus pallidus to the red nucleus along with inputs from the motor cortex and the deep cerebellar nuclei are believed to modulate the tone of flexor muscles. The tectospinal tract that arises from the midbrain tectum, consists of crossed fibers, ends on the interneurons, and influences the movements of the head and body with respect to visual stimulus. In general, the extrapyramidal tracts that influence the axial muscles are largely uncrossed while those influencing the muscles of the limbs are mostly crossed. Such an arrangement permits the independent control of the limbs and axial muscles so that the manipulations can proceed while the posture is maintained.

Basal ganglia were believed to exert an inhibitory influence on the motor system. However, recent researches suggest the presence of both excitatory and inhibitory influences. In addition to the above, the input from the cortex also seems to have priority over the input from the thalamus and substantia nigra and provides certain evidence that the cortex is involved in regulating the responsiveness of the caudate neurons. Basal ganglia stimulation may prepare the cortex for subsequent inputs and activate only the most necessary pathways and inhibit all unnecessary pathways.

4.1.1 Direct and Indirect Pathways

The direct and indirect pathways are the two distinct pathways that process signals through the basal ganglia. Both pathways work in conjunction with each other. Excitation of the direct pathway has the net effect of exciting the thalamic neurons and the excitation of the indirect pathway has the net effect of inhibiting the thalamic neurons. Though the pathways have opposite net effects, a fine balance exists between them for the normal functioning of the basal ganglia. Current literature believes that an imbalance between these two pathways is responsible for the hypokinetic or hyperkinetic movement disorder seen in basal ganglia disorders. For instance, a less active direct pathway or an overactive indirect pathway can reduce cortical activation, causing bradykinesia and akinesia (hypokinetic movement disorders). Alternatively, an overactive direct pathway or less active indirect pathway can facilitate cortical activation, causing hyperkinetic movement disorders.

The direct pathway is a cortico-basal ganglia-thalamo-cortical loop that passes through the striatum, pallidum, substantia nigra, and thalamus to the cortex (Fig. 4.5). By default, the thalamic nuclei (Ventral Anterior nucleus [VA] and Ventral Lateral nucleus [VL]) are inhibitory to the cerebral motor cortices. In a normal

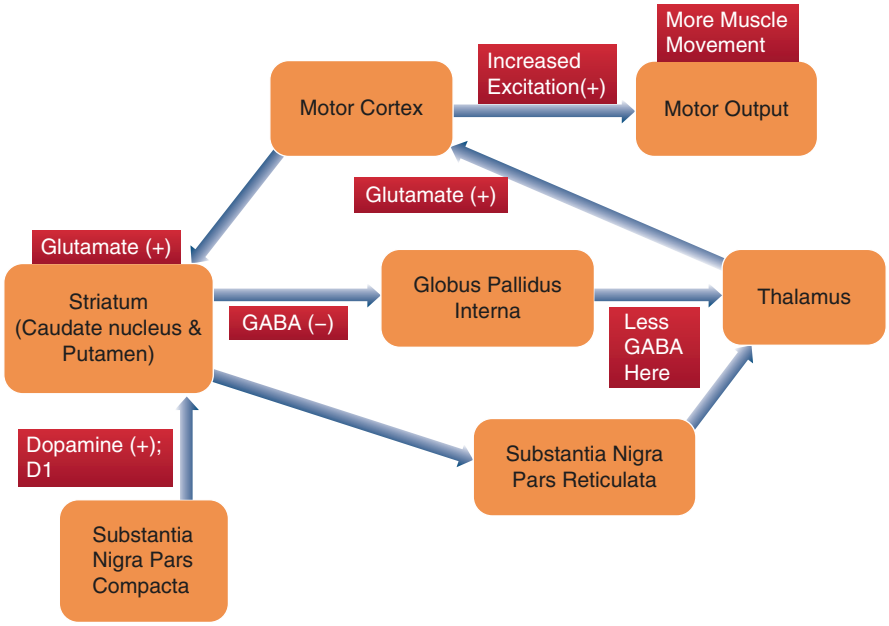

Fig. 4.5 Flowchart depicting the direct pathway

situation, during the activation of the direct pathway, the cerebral cortex excites the striatum through glutamate release. Inhibitory neurotransmitters (Gamma-aminobutyric acid [GABA]) released from the excited striatum inhibit the globus pallidus interna, a part of pallidum, and the pars reticulata, a part of substantia nigra. Inhibition of the globus pallidus interna and the pars reticulata reduces the inhibitory signals to the thalamus nuclei. Inhibition of the inhibitory neurons that project from the thalamic nuclei to the cerebral cortices thereby facilitates and promotes muscular action.

The indirect pathway passes through the striatum, globus pallidus externa, traverses the subthalamic nucleus, enters the globus pallidus interna and then the thalamus, and ends in the cerebral motor cortex (Fig. 4.6). In a normal situation, when the indirect pathway is activated, the release of glutamate from the cerebral cortex will excite the striatum. The excited striatum will release GABA, which in turn will inhibit the globus pallidus externa. The inhibition of the externa reduces the release of GABA, which is inhibitory to the subthalamic nucleus. Less inhibition of the subthalamic nucleus will cause more glutamate release, which is excitatory for the globus pallidus interna. Excitation of the globus pallidus interna will inhibit the thalamic nuclei, in turn inhibiting the cerebral cortices leading to the reduction of muscular activity.

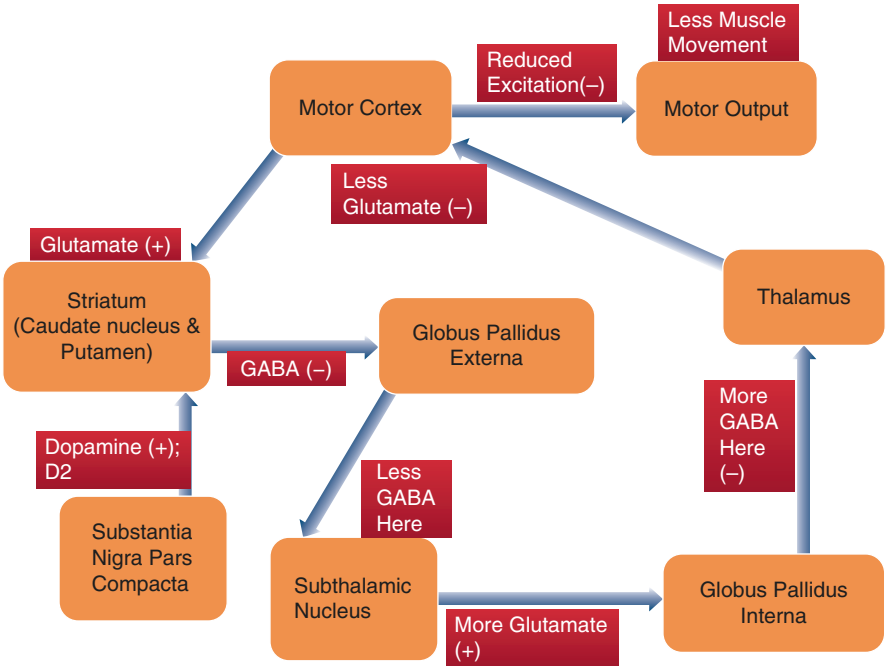

Fig. 4.6 Flowchart depicting the indirect pathway

4.1.2 Neurotransmitters Within Basal Ganglia

Dopamine, acetylcholine, GABA, substance P, enkephalins, and endorphins are certain common neurotransmitters seen in high concentrations within the basal ganglia. Dopamine, a major neurotransmitter of the nigrostriatal pathway, is produced by the pars compacta of the substantia nigra. The axon terminals of these dopaminergic neurons are located in the caudate nucleus. Dopamine is excitatory to the neurons in the direct pathway and inhibitory to the neurons in the indirect pathway. The loss of dopamine in the direct pathway leads to loss of excitation of the direct pathway and excess of excitation of the indirect pathway and reduction in activation of the thalamocortical pathway. Basal ganglia consist of several dopamine receptors and dopamine is also known to modulate the effects of other neurotransmitters, including glutamate.

Acetylcholine (ACh), another neurotransmitter found in the small interneurons of the striatum, is presumed to inhibit the action of dopamine in this region and is classically in tune or balance with the latter. An imbalance between ACh and dopamine is believed to be a plausible cause for the development of movement disorders like Parkinson's disease (PD). GABA, an inhibitory neurotransmitter found throughout the brain, is synthesized by the caudate nucleus and is transmitted to the globus pallidus and substantia nigra. The reduction of GABA in the indirect pathway and imbalanced dopamine activity are possible reasons for the choreiform movements in the early stage of Huntington's disease. Decreased GABA in the direct pathway and imbalanced dopamine activity are the plausible reasons for the rigidity and bradykinesia in the later stages of Huntington's disease.

4.1.3 Basal Ganglia: Posture and Movements

Experimental ablations of different parts of basal ganglia in animal models were extensively performed in the eighteenth and nineteenth centuries. Such ablations in animal's motor models have produced a variety of motor behavioral responses varying from no visible response to abnormal twisting and posturing of the body or body parts. By the nineteenth century, the use of electrical stimulation provided more insight into the functioning of basal ganglia. With sufficient intensity, the caudate nucleus stimulation could produce total body movement patterns and postures, usually a generalized flexion response of the head, trunk, and limbs.

Basal ganglia are implicated in aspects of the initiation and execution of movements, as well as in postural processing and postural adjustments. Many researchers agree that the basal ganglia are involved in movement initiation and preparation. Few of the researchers even recorded a possible "readiness potential" from the scalp of normal subjects that were absent in PD patients. They hypothesized that these potentials were generated from the basal ganglia and not from the motor cortex. More recent studies implicate that lack of these readiness potentials could be the

possible cause of initiation difficulty in PD. People with basal ganglia disorders typically assume flexed or stooped postures and have decreased postural stability and a higher risk for falls. These patients often have reduced static postural adjustments. Research studies have also pointed out abnormalities in the reflexes involved in postural adjustments and spotted deficits in the longer loop reflexes but not in the short-latency reflex associated with the stretch reflex. Such deficits may reduce the person's ability to precisely modify the postural responses to the environmental demands and may predispose to abnormal postural reactions and even falls.

The integration of sensory information is essential to perform cognitive activities. Lesions of basal ganglia can produce poor sensory integration and cognitive functions, predisposing to abnormal movements and postures. Studies had proven impaired kinesthesia in basal ganglia disorder patients and also found that the impairment increased when they moved their limb further away from the body's center. Studies also found that learned movements were more affected by ganglia lesions than reflexes, particularly the procedural learning that is often needed to develop habits. Habits are easy to perform and such activities can proceed without thought or a conscious effort, allowing the person to think and react freely to new situations, enabling the person to select the appropriate movement in the proper environmental context.

The bilateral integration of the body is important for movements to be controlled and appropriately sequenced. Anatomical evidence suggests that the basal ganglia may have certain means of bilateral control, for the same reason, persons with basal ganglia disease may reveal function deficits even on the unaffected side and may exhibit difficulty in performing bilateral asymmetric movements simultaneously.

The primary function of the basal ganglia is to control and regulate the activities of the motor and premotor cortical areas and help to choose the right motor behavior from several possibilities at any given time. The functions may also include preparing the cortex for approximate time activation, setting appropriate postural reactions, sensory input organizing to produce an appropriate motor response that is context-specific, and inhibiting unnecessary motor activity. Earlier, the functional organization of the basal ganglia was believed to be a loop mechanism where afferent activity from the cortex is processed and modulated by the basal ganglia and subsequently sent back to the cortex to either facilitate or inhibit motor activity. However, the current concepts believe that the basal ganglia have several loops, where the cortical and the subcortical projections interact with the internal loops, forming a complex network, designed for selecting and inhibiting simultaneously occurring events and signals (Fig. 4.7).

Pathology affecting any of the motor projections or loops encompassing the basal ganglia can result in a spectrum of movement abnormalities ranging from excessive involuntary movements that may interfere with normal functioning (hyperkinetic or dyskinetic) to slowness or total poverty of voluntary movements (hypokinetic or akinetic). The details regarding the common movement disorders seen in basal ganglia pathologies are listed in Table 4.1.

The extrapyramidal disorders are either primary or secondary in origin. Progressive idiopathic neurodegenerative disorders like idiopathic Parkinson's

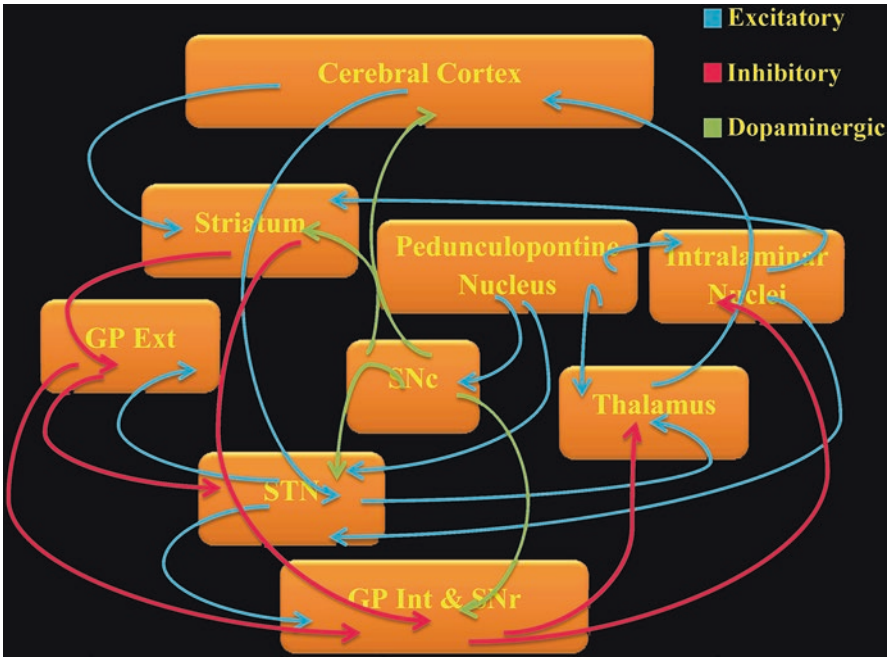

Fig. 4.7 Facilitatory, inhibitory, and dopaminergic loops operating at the basal ganglia

disease, Shy–Drager syndrome, progressive supranuclear palsy, and progressive genetic neurodegenerative disorders like Wilson's disease and Huntington's chorea are primary extrapyramidal disorders. The secondary causes of extrapyramidal disorders can be due to toxins or drugs, metabolic, vascular, space-occupying, trauma, and infections. Table 4.2 shows the clinical differences between extrapyramidal and pyramidal (corticospinal) disorders. This chapter will cover all the common and some unique disorders of the basal ganglia which affect the adult population.

4.2 Idiopathic Parkinson's Disease

In 1817, James Parkinson, a general practitioner and a surgeon in the countryside of London, published a monograph called "the shaking palsy." In his original description about shaking palsy, also known as paralysis agitans, features like involuntary tremors, reduced muscle power, bend or stooped trunk, tendency to pass from a walking to a running pace, and intact sense and intellect were mentioned. He also considered that the disease was of brainstem origin. Several decades later, Jean-Martin Charcot, also known as the father of modern neurology, renamed this condition as Parkinson's disease.

Table 4.1 Listing the common movement disorders of the basal ganglia, their features, and the location of the lesion

Movement disorder	Definition/features	Location/possible location/ cause
Ballismus	Involuntary, purposeless, jerky, wild, flinging movements of an entire limb; ballistic movements are usually unilateral (hemiballismus); flinging movements can be continuous or intermittent and can be unsafe or often cause falls.	Lesion in and around the surrounding areas of subthalamic nucleus
Tics	Stereotyped, repetitive irresistible movements that tend to change in type and anatomical location over long periods of time; typically seen as actions like repeated clearing the throat, protrusion of chin, sniffing, and blinking; often compelled to make these movements to relieve perceived tension; can be suppressed for a short time by will and may reappear when the subject's attention is diverted.	No known pathologic location in the basal ganglia or other locations of the brain
Chorea	Involuntary, purposeless, frequent, brief, sudden, twitch-like movements that flow from body part to body part; seen proximally or distally; large or small in amplitude; intermittent or nearly continuous.	Usually in the caudate nucleus or the striatum
Athetosis	Involuntary, purposeless, slow, often complex, writhing movements of the extremities; distal more than proximal; particularly of the hand, forearm, and arm and in some cases, lower extremity, neck, and tongue.	Common in lesions of striatum; pathological changes are seen more in the putamen than in the caudate nucleus
Myoclonus	Involuntary, quick, irregular twitching of a muscle or a group of muscles; intensity and frequency can be variable from case to case; may affect one or more body parts.	Usually diffuse or predominantly in cortical, subcortical, or cerebellum
Resting tremor	Involuntary repetitive, rhythmic, oscillatory movements; observed when the patient is at rest; usually seen in distal parts of extremities, jaws, lips, and tongue; frequency in the 4–6 Hz range; episodic in time; suppressed or enhanced by motor or cognitive activity	Localization of the central oscillator is still debatable; either basal ganglia or thalamic origin; may extend beyond basal ganglia circuitry
Bradykinesia	Slowness in both initiation and execution of movement	Dopamine (produced by nigral cells) is essential for modulation and facilitation the striatum; Reduced GABAergic transmission through the direct pathway and increased GABAergic transmission through the indirect pathway

(continued)

Table 4.1 (continued)

Movement disorder	Definition/features	Location/possible location/ cause
Dystonia	Involuntary muscle spasms, producing repetitive or twisted postures of different parts of the body; spasms can range from mild to severe; can affect one body part focal dystonia), two or more adjacent parts (segmental dystonia), or all parts of the body (general dystonia); precipitated by certain specific actions like handwriting; worsened with stress, fatigue or anxiety.	Focal lesions in the putamen, globus pallidus, or thalamus; different nuclei of the basal ganglia are emphasized
Rigidity	A form of muscle hypertonia, characterized by stiffness of muscles and difficulty to move the joints passively; resistance is felt in both the agonists and antagonist, however, can be more profound in one group-usually flexors; unlike spasticity, the resistance is not velocity dependent; the presence of normal tendon jerks; may reduce the range of motion of the joints; either cogwheel or lead pipe in nature; stress and anxiety may worsen rigidity	Hyperexcitability in long loop reflex pathways
Akinesia	An inability to initiate with absolute poverty of movement, characterized by a complete loss of voluntary movement in the absence of paralysis; considerable effort and mental concentration required to produce even the simplest motor activity.	

Table 4.2 Listing the clinical differences between extrapyramidal and pyramidal disorders

Clinical feature	Extrapyramidal	Pyramidal
Muscle tone	Plastic, lead pipe rigidity (resistance equal throughout the passive movement), or cogwheel rigidity (resistance with waxing and waning)	Clasp-knife type and velocity-dependent hypertonicity
Distribution of tone	Generalized hypertonicity, however, predominates in flexors of limbs and trunk	Flexors of arms, extensors of legs
Abnormal or involuntary movements	Presence of resting tremor, ballismus, chorea, tics, athetosis, and dystonia	Absent
Deep tendon reflex	Normal or occasionally brisk	Brisk or exaggerated; Sustained or transient clonus may accompany
Babinski sign	Absent	Present
Voluntary movements	Present, but can be hyperkinetic or hypokinetic	Absent/reduced; based on the extend of corticospinal tract lesion.

Idiopathic Parkinson's Disease (IPD) is the most common progressive degenerative neurological condition after Alzheimer's disease. Typically, the natural history of the disease begins between the fifth and seventh decades of life. The disease is more frequent among men than women and the ratio is approximately 3:2. Though the cause of IPD is unknown, physical trauma, exposure to certain unidentified environmental toxins, rigid personality, overwork, exposure to cold, emotional troubles, and stress can be some of the important factors predisposing to the disease. However, there is no conclusive evidence to support such assertions. The IPD is seen in all parts of the world and all races. At any given time, IPD affects 1–2 per 1000 of the population and affects approximately 1% of the population over 65 years of age. In most cases, the disease has no genetic or familial predisposition. At the same time, the role of genetic factors cannot be ruled out as dopamine metabolism utilizing Positron Emission Tomography (PET) scanning on asymptomatic twins of diagnosed IPD cases revealed evidence of striatal dysfunction.

4.2.1 Clinical Features of Idiopathic Parkinson's Disease

Typically, the symptoms of IPD emerge slowly. Resting tremor, bradykinesia, rigidity, and postural reflex disturbance are the major motor symptoms. The core symptoms consist of resting tremor, poverty and slowness of voluntary movements (bradykinesia), stooped posture, mask-like expressionless face (hypomimia), rigidity, axial instability, and Parkinsonian or festinating gait. During the very early stage of the disease, the symptoms are often difficult to perceive and both the patient and the family members may attribute those to the effects of aging. Often during the early stage, the patient may have vague complaints of fatigue and weakness, cervical and low back pain, shoulder and hip pain, and a general slowing up of physical activity. Gradually typical features like resting tremor and voice change will emerge. The patient's voice may progressively become soft and monotonous. Mild stiffness and slowness of movement, reduction in the natural swing of arms while walking are usually ignored or not bothered with until one day it draws the attention of the physician or family members as the possible inroads of the disease.

As the disease progresses, the progressive changes in gait may become noticeable, including short steps, hurrying, and shuffling. Facial expression reduces and often, the mouth is left slightly open. The blink rate will be reduced to 5–10 instead of a normal blink rate of 12–20 per minute. In addition to the hypomimia, a reduced blink rate with widened palpebral fissures creates a staring gaze known as the Stellwag sign. The weight shifts and adjustment movements, which are seen in normal subjects while seated, are progressively and markedly reduced in IPD patients. In most patients, olfactory dysfunction is one of the earliest non-motor features of IPD; however, total anosmia is rare.

The patients or family members may report the tremors involving the distal aspect of the upper extremity, mainly the hand. Such tremors can be an early sign and in the early stage of its development, be mild and intermittent, often seen only

in a few fingers or one hand. Over a period, the tremor can develop into a full form, including the classical pill-rolling tremor of the thumb and fingers. Typically, these tremors, known as "resting tremors," are present when the body part (usually distal: hand or foot) is at rest and motionless. Sleep can abolish, and relaxation and voluntary movements can considerably reduce or eliminate these tremors. Distraction, simple mental arithmetic, or counting with the eyes closed can bring out these tremors when they are less observable. Though the resting tremors are common in the hand and foot, careful observation may reveal such tremors even in the arm, jaw, tongue, and eyelids. The frequency of the resting tremor is usually between 4 and 6 Hz. The resting tremor may worsen with gait or emotional upset; however, the frequency will remain largely unchanged.

The IPD patients may present with another tremor known as action tremor. Action tremors are finer and have a frequency of 7–8 Hz. They tend to persist throughout the voluntary movement and are easily suppressible by relaxation and unnoticeable when the limb is essentially at rest. IPD patients may have resting and/or action tremors. Electromyographic studies of both the tremors mentioned above have proven that the muscle activities recorded were not exactly the same. However, studies have shown certain similarities between the action tremor and the essential tremor.

Unilateral onset is typical of IPD, i.e., the motor impairments and resting tremors tend to develop in one limb or one side of the body and may spread to other regions as the disease progresses. Both rigidity and muscle hypertonicity are not early findings and tend to develop as the disease advances. Once they appear, they are constantly present. Hypertonicity tends to predominate in the flexor muscles of the trunk and limbs and is possibly responsible for the flexed or stooped posture, typically seen in IPD. Even when the patient is well relaxed, on palpation, the muscles may appear unusually firm and hard. Irrespective of the direction of the movement, when the limbs are passively moved, a mild resistance will be felt from the start and continues evenly throughout the movement. The resistance felt during the passive movement can be lead pipe (resistance is equal throughout the passive movement) or ratchet-like cogwheel (resistance with waxing and waning) sensation.

Difficulty or inability to perform ballistic movements is another volitional movement abnormality seen in IPD patients. Typically, the movements are initiated slowly and may demonstrate a series of attempts to initiate, when quick or fast movements are tried. While performing alternating movements, observation of the ongoing movement may reveal a progressive failure in continuing alternate movement or adaptation of a rhythm similar to the patient's own tremor. Further, during the advancement of the disease, the patient will develop difficulties in executing two or more motor tasks simultaneously.

As the disorder progresses, the movement abnormalities, specifically bradykinesia, worsen and affect a variety of functional activities. The handwriting progressively becomes small (micrographia), tremulous, cramped, and illegible. The voice softens further and speech becomes hurried, more monotonous, less audible, indistinct, and mumbling ("hypokinetic dysarthria") and eventually, the patient can only

whisper. Bradykinetic deficits, along with rigidity, can cause swallowing difficulties and slowness of chewing and as a result, the patients may take considerable time to finish feeding.

Camptocormia, a severe flexion attitude of the thoracolumbar spine in the sagittal plane, typically more than 45°, while standing and walking and almost completely resolving in the recumbent position, can be a feature of postural abnormality in the advancing stage. The patient may develop other postural abnormalities like scoliosis and antecollis. Antecollis consists of severe forward flexion of the head in the sagittal plane, with the inability to voluntarily fully extend the neck against gravity. It is more frequent in multiple system atrophy than in PD. Another frequent and disabling postural abnormality seen among PD patients is the Pisa syndrome. It is characterized by a marked lateral flexion of the trunk (a Cobb angle of more than 10°), which is completely reversible by passive mobilization or supine position.

In addition to reducing postural adjustment capacities, as the disease advances, righting reactions and the body's defense mechanisms like equilibrium reactions and protective reactions become progressively faulty. Postural instability and gait failure are the most disabling features of IPD. Progressive changes in gait such as a tendency to pass from a walking pace to a running pace with forward bent trunk posture, increased cadence, reduced step and stride length, narrow base of support while walking, lack of arm swings, absence of rotation and counter-rotation of the upper trunk with respect to the lower trunk, reduced velocity, poor ground clearance and tendency to shuffle are certain important features of the festinating gait. The patients may tend to fall forward or backward if pushed or pulled (propulsion or retropulsion). While walking, they may topple forward with faster steps and have difficulty stopping (festination). A history of falls, either forward or sideways, is not uncommon. Walking forward or backward is difficult and may be accomplished with a series of short steps and as the disease advances, the gait develops into the typical slow shuffling walk with small steps on a narrow base.

In the advanced stage, negotiating obstacles, turns, and cluttered spaces, and walking in crowded places or narrow passages causes freezing of gait. Even basic activities like turning over in bed will be difficult, effortful, and time-consuming owing to the bradykinesia, rigidity, and impaired righting reactions. Persistent clawing of the toes or jaw clenching and similar features of dystonia, which are often painful, may be evident in the advanced stages. Even eye movements are bradykinetic, characterized by a delay in the initiation of gaze, slowness in producing conjugate gaze movements, and hypometric in saccadic movements with a breakdown of pursuit movements into small saccades.

The advent of dementia during the advancing stage further complicates the disease. It is estimated that 20–30% of patients will become demented. The incidence of dementia tends to increase with the advancement of disease and age. Approximately 65% of PD patients above the age of 80 years have a certain amount of dementia. Often, depression and neuropsychiatric side effects of medications can make the clinical detection of dementia difficult. Development of dementia, along with cognitive slowing, depression, and memory impairment in the absence of aphasia and agnosia, is typical in the advancing stage.

In the later stage, the drooling of saliva (sialorrhea) can be troublesome. Reduced swallowing due to bradykinesia and rigidity of the muscles of deglutition and excess flow of saliva are the possible reasons for this. These patients often have seborrhea (excessive production of sebum from the sebaceous glands) that makes the skin more greasy or oily. Hyperactivity of the parasympathetic system and/or overactivity of androgens are possible factors attributing to seborrhea. In addition to the above, these patients also have excessive sweating due to lack or failure to cleanse the face regularly and sufficiently, and owing to constant motor activity. Orthostatic hypotension and syncope can be clinical features due to neuronal cell loss in the sympathetic ganglia. Constipation, another common autonomic dysfunction, if severe, may require frequent hospital admission. However, it is not a prominent feature, as seen in the Shy–Drager syndrome.

Clinical examination of the IPD patient will reveal the presence of Myerson sign or glabellar tap sign (inability to resist blinking of the eyes when tapped repetitively over the bridge of the nose or glabella), absence of palmomental, grasp, and suck reflexes and absence of exaggerated jaw jerks. The deep tendon reflexes vary and range from barely elicitable to brisk. Whether symptoms are confined to one side or equal on either side of the body, the plantar responses are flexor in nature.

The disease course is quite variable. The mean time from the commencement of symptoms of the disease to a wheelchair-bound state is approximately 7.5 years in the majority of patients. Whereas, as many as one-third of the cases with relatively mild features may remain stable for 10 years or more, indicating a vast variation in the course duration of the disease. The cognitive decline associated with dementia and the older age of onset were recognized as the predictors of reduced survival time.

4.2.2 Clinical Diagnosis

If one strictly adheres to the definition of PD, in the majority of cases, the clinical diagnosis is quite straightforward. The presence of two out of the three cardinal features—bradykinesia, rigidity and tremor, presence of postural instability, a good clinical response to levodopa therapy and absence of any “atypical” features suggestive of another Parkinsonian syndrome makes errors in diagnosis less likely. The presence of small signs such as reduced blink rate, the Myerson sign and the Stellwag sign and absence of the Babinski sign, hyperactive deep tendon reflexes in the affected limbs, and suck, grasp, and palmomental reflexes may further help in the diagnosis.

Occasionally, the clinicians may face difficulty in distinguishing a typical IPD from the many Parkinsonian syndromes, particularly when all the signs and symptoms are not evident at the outset. In such situations, re-examining such cases after several months may bring better clarity about the impending medical condition. The presence of symmetrical features and rapid onset and progression of the clinical

features right from the inception are unlikely to be IPD. Reduction of clinical features such as gait and postural instability and bradykinesia post lumbar puncture and absence of features like forward stooped posture, resting tremor, and a positive response to levodopa therapy helps to distinguish normal-pressure hydrocephalus from IPD. Similarly, some of the features of progressive supranuclear palsy can often be mistaken for IPD. The presence of early falls, with a predilection to fall backward, paralysis of upward and downward gaze, and eventually the lateral gaze with retention of reflex movements of the eye are definite features of progressive supranuclear palsy, unlike IPD.

4.2.3 Etiology, Neuropathology, and Neuropathogenesis

The etiology of PD is most likely multifactorial. Mitochondrial dysfunction, along with free-radical damage and the presence of neuroinflammatory changes, appears to play an important role in the pathogenesis of PD. A presynaptic neuronal protein named α-synuclein, genetically and neuropathologically linked to PD, may also be playing a central role. Misfolding and aggregation of the α-synuclein is a hallmark of PD. The questions of whether neuroinflammation triggers α-synuclein misfolding and aggregation or does misfolding and aggregation of α-synuclein cause microglia activation and neuroinflammation are largely unclear. Similarly, the exact mechanism by which α-synuclein causes cellular toxicity and contributes to neuronal death remains unclear.

Typically, the naked eye examination of the brain will not show any remarkable findings. However, IPD patients with associated dementia may have a mild to moderate degree of cerebral atrophy. The most persistent and relevant neuropathological findings in IPD are the loss of pigmented dopaminergic neuronal cells in the substantia nigra pars compacta associated with the presence of intraneuronal inclusions called Lewy bodies.

Though aging contributes to nigral cell loss, the cell depletion is considerably marked in IPD, indicating that some factors other than aging must be operative. It is estimated that at least 50–70% of nigral cell degeneration is required to produce symptoms of the disease. The nigral cell loss is initially rapid and later slows down with time. In addition to the nigral cell loss, there is a significant neuronal loss within the locus ceruleus, the dorsal motor nucleus of the vagus, the raphe nuclei, and the nucleus basalis. The presence of reactive gliosis accompanying neurodegeneration, Lewy bodies in other locations, including subcortical structures and neuromelanin released from dying neurons of pigmented nuclei, are some additional microscopic observations. The presence of Lewy bodies is not absolutely specific to IPD as these bodies are also seen in other neurological disorders such as the Parkinsonian variant of multiple system atrophy and Lewy body dementia.

4.2.4 Medical and Surgical Management

Immediate drug treatment is often not required or postponed for elderly patients who present late, with no marked disability at the time of diagnosis. To date, no definitive treatment, medical or surgical, that can reverse or halt the progressive neuronal cell loss underlying IPD has been neither discovered nor invented. A careful explanation of the diagnosis, treatment options, and prognosis by the neurologist and reassurance that early medications would not have influenced the situation and no treatment will completely suppress all symptoms, helps to avoid premature drug therapy and pointless overmedication.

Neuroprotective therapy for those patients not requiring symptomatic medications in the early stage, symptomatic therapy when symptoms begin to disable or disturb, and management of treatment-related complications and drug-resistant features in the advanced stage of the disease are the preferred three stages of treatment. Selegiline, a neuroprotective drug, widely used in early Parkinson's, is believed to prevent intracerebral metabolic degradation of dopamine. Clinical trials conducted by the Parkinson Study Group revealed a slow progression of the disease; however, subsequent observations of other trials could not corroborate with the earlier findings. Even the use of vitamin antioxidants like Vitamin E to reduce nigral oxidative damage has not revealed any beneficial effect on the disease progression. Coenzyme Q10, known as a mitochondrial nutrient with free radicals scavenging capacity, is another neuroprotective drug. Administration of coenzyme Q10 is found to benefit several mitochondrial-defective diseases, including PD, particularly in the early stages.

When the symptoms are disabling, the use of Parkinson's medication to control the symptoms is preferred. Levodopa, non-dopaminergic drugs such as anticholinergics and amantadine, and dopamine agonists are the classes of Parkinson's medications. Non-dopaminergic drugs are preferred for mildly affected patients and help to delay the early prescription of levodopa or dopamine agonist. Anticholinergics help prevent the imbalance between ACh and dopamine in the striatum and are effective in suppressing resting tremors when tremors are a major concern than bradykinesia. The mode of action of amantadine is more complex and is believed to increase the presynaptic dopamine re-uptake and release. Insomnia, agitation, confusion, and pedal edema are some of its side effects.

For patients with significant disabilities, dopaminergic treatment is the choice. The theoretical basis for the use of levodopa, the most effective Parkinson's medication, rests on the observation that the ability of the remaining nigral cells to convert levodopa to dopamine is not significantly reduced by the progressive loss of nigrostriatal cells. To increase the bioavailability of orally administered levodopa, reduce peripheral conversion of dopamine, and minimize the side effects like nausea and vomiting, a peripherally acting decarboxylase inhibitor (carbidopa or benserazide) is given as a combination. Levodopa is highly effective against tremor, rigidity, and akinesia and is undoubtedly the most effective treatment for IPD. However, with the progression of the disease, the drug response reduces, and higher dosages when

required are associated with serious long-term issues. When the number of remaining nigral cells becomes inadequate and the receptivity to dopamine becomes excessive due to denervation hypersensitivity, the beneficial effects of levodopa will reduce and adverse effects like dyskinesia will begin. Within 5 years post-diagnosis, 50% of IPD patients will experience adverse effects and almost all by the next 5 years. Progressive shortening of the response to each dose leads to the "wearing off effect" or "end of dose deterioration" and is characterized by the reappearance of Parkinson's features before the next dose is due. Sooner or later, the patient frequently switches between drug "on" state (associated with dyskinetic movements) and drug "off" stage (severe rigidity and akinesia). Increasing dopaminergic nigrostriatal cell destruction and reducing presynaptic storage of dopamine are the possible reasons for the drug on-off phenomenon.

To prevent the early onset of long-term levodopa-related adverse effects and as an alternative to levodopa, dopamine agonist monotherapy is employed. Bromocriptine, pergolide, and lisuride are certain dopamine agonists. Overall, dopamine agonist monotherapy is associated with a much lower incidence of dyskinesia and motor fluctuation; however, it has its own side effects like nausea, hypotension, and confusion. Dyskinesias are often difficult to treat and are characterized by restlessness, head wagging, grimacing, lingual-labial dyskinesia, and dystonic posturing of extremities and spine. Only about 50% of the patients, especially patients with early Parkinson's, can tolerate dopamine agonists.

Severe off periods can be extremely unpleasant with rigidity and akinesia, restless limbs, sweating, pain, and autonomic abnormalities. In advanced PD, increasing the frequency of levodopa, finding a levodopa dose that provides the best balance between Parkinsonism and dyskinesia or the introduction of a dopamine agonist and reduction in levodopa dosage may reduce the levodopa-related complications and emerging drug-resistant features. Parkinson's medication can improve gait abnormalities, freezing of gait, and falls to some extent, but the improvement is usually modest at best.

Early neurosurgical treatment, even before the advent of levodopa therapy, revealed only limited improvement and had considerable morbidity. Thalamotomy was effective for tremor but had little impact on bradykinesia and rigidity. Later, after the advent of stereotactic surgeries, stereotactic thalamotomy of the nucleus ventralis intermedius continued to show a certain role in early Parkinson's with severe tremor. Stereotactic pallidotomy is increasingly used in suppressing dyskinesia; however, studies have shown no significant improvement for postural, gait, and speech abnormalities.

Deep brain stimulation was a recent addition and alternative management to stereotactic brain surgeries. The advantage of deep brain stimulation over stereotactic lesions is that the former is reversible and is safer. Deep brain stimulation of the thalamic nucleus ventralis intermedius has demonstrated success in reducing tremor and dyskinesia. Stimulation of the globus pallidus interna or subthalamic nucleus has shown a reduction in all symptoms. Some of the complications that have been reported post-stimulation include weight gain, mild dystonia, eyelid apraxia, hemorrhage, infection, and cognitive impairment. Another neurosurgical

development has been the use of transplanted fetal mesencephalic neurons into the striatum of patients with advanced PD. Post-transplantation, levodopa requirements were reported less in some patients, but few studies have shown only a modest improvement.

4.2.5 Physiotherapy for Parkinson's Disease

Physiotherapy has a central role in reducing activity limitations, promoting participation and functional independence, and enhancing safety and well-being. To deliver optimal care to PD patients and address all the issues, the physiotherapist needs adequate knowledge about the disease, the clinical manifestations, and specific physiotherapy skills. The common principle for physiotherapy is that the therapy should be patient-centered and tailored to the patients' specific needs and preferences. It is also essential to empower the patients by education and enable them to continue the training program even when the therapist-supervised session is completed for the day.

The exercise training program should consider the history, disease course, severity of impairments, activity limitations, and participation restrictions. Depending on the stage of the disease, the physiotherapy interventions can be restorative (for reducing impairments, activity limitations, and participation restrictions), preventive (for minimizing potential complications and indirect impairments), and compensatory (for functional improvement by modifying the task, activity, or environment). During the early phase (1–2.5 stages of Hoehn and Yahr scale) of PD, the majority of the patients are functionally independent with minimal impairments. The goals of the therapeutic intervention for the early phase are to prevent inactivity and preserve or improve physical capacities such as aerobic capacity, muscle strength, and joint mobility. A referral for physiotherapy at this stage will certainly benefit the patient to improvise his or her physical fitness levels and delay or prevent the early onset of indirect impairments. At this stage, such patients are mostly seen on an outpatient basis.

In the middle stage or phase (2.5–4 of Hoehn and Yahr scale) of the disease, symptoms are more readily noticeable and the emergence of activity limitations also characterizes it. The patient is typically still independent in gait and Activities of Daily Living (ADL), although slow and less efficient in performance. The goal of therapeutic intervention in this phase is to preserve or encourage activities. The therapy should focus on specific issues like transitions within the bed and off the bed, static and dynamic postures, balance, and gait. Cognitive movement strategies and cueing strategies can be effectively utilized during this stage and even the family members can be actively involved during this stage of treatment. Usually, patients in the middle stage of PD are treated on an outpatient basis or following a brief inpatient admission or as a part of home care. During the late phase (fifth of Hoehn and Yahr scale), the disease progression leads to more severe complications and impairments. For many of the functional mobility skills and ADL, the patients are

more or less completely dependent and are either wheelchair-bound or bed-confined. For such patients, the physiotherapy goals need to be restructured and should focus on preventative care to avoid secondary complications, including life-threatening complications like bronchopulmonary pneumonia or decubitus ulcers.

Resting tremor, bradykinesia, and rigidity are considered to be the direct or primary effects caused by the progressive degeneration of the nigrostriatal dopaminergic cells of the central nervous system. The involvement of a system other than CNS, like musculoskeletal or cardiopulmonary, gives rise to symptoms like kyphosis, contracture, reduced mobility, urogenital issues, and cardiopulmonary deconditioning, known as the indirect or secondary effects of the disease. Symptoms like abnormal posture, faulty balance, swallowing difficulty and fatigue, arise due to composite involvement of CNS with one or more other systems, known as the composite effects of the actual disease. The therapist should have a comprehensive understanding of the direct, indirect, and composite effects of the disease. Concerning the therapy, in the early and middle stages of the PD, symptoms arising due to secondary and composite effects of the disease are often amenable to corrective or preventive strategies. However, in the later stages (fourth and fifth of Hoehn and Yahr scale), "little can be done for symptoms due to actual disease" and the benefits of corrective or preventive strategies for secondary and composite effects are rather short-lived.

4.2.5.1 Assessment

The information obtained while taking the patient's history should help to formulate the objectives of treatment and be the basis for focusing the physical examination on specific areas of functioning, namely physical capacity, transfers, body posture, balance, and gait. A comprehensive clinical examination is essential to determine the level of impairments and activity limitations and participation restrictions (Table 4.3). Periodic re-examinations at specific intervals (approximately 3–6 months for early and middle stage PD) are worthwhile to distinguish the changes in physical and functional status and for restructuring the goals and means of therapy.

Considering the attention and emotional deficits, the clinical examination of the PD patients should be preferably executed in a quiet room. The fear of falls and the associated anxiety can be alleviated by performing the examination on a low height, broad examination table. During the physical examination, the therapist should note whether the patient is in a drug "on" or "off" phase. Also, it is essential to note down the details regarding the medications, specifically emphasizing the dosage, timings of medication, and the time of the last administration. The selection of procedures and instruments for examination is determined by the patient's age, status, severity of complaints, stage of the disease, phase of rehabilitation, and location of rehabilitation. For both the early and middle stages of PD, physical performance and impairment measurements are relatively stable. However, in the late stage, fluctuating symptoms and adverse effects of pharmacological intervention make measurements less reliable.

Table 4.3 Details regarding the level of impairments and activity limitations and participation restrictions in Parkinson's disease

Impairments in functions			Activity Limitations and restrictions in participation
Neuromusculoskeletal and movement-related functions	Reduced joint mobility, muscle endurance, muscle power, postural responses and control of voluntary movements; impaired muscle tone functions and motor reflex functions; involuntary movement functions and gait patterns; on/off periods		• Mobility: Changing and maintaining body positions; carrying, moving, and handling objects; walking and moving; using transportation • General tasks and demands: Undertaking multiple tasks; handling stress and other psychological demands • Self-care: Washing oneself; toileting; eating; drinking • Learning and applying knowledge: Acquiring skills; making decisions; writing solving problem • Interpersonal interactions and relationships • Communication: Speaking; non-verbal and writing messages • Domestic life: Preparing meals; doing homework • Major life areas: Education; work; employment; economic life • Community, social and civic life: Community life; recreation and leisure; religion; political life
Mental functions	Delirium; Dementia; Impairments in temperament and personality, energy and drive functions, sleep, emotion, perceptual functions higher-level cognitive functions and mental functions of language; reduced attention and memory		
Voice and speech functions	Reduced pitch, loudness of voice and fluency of speech; impaired articulation		
Cardiovascular and respiratory systems functions	Impairments in blood pressure; reduced exercise tolerance		
Sensory functions and pain	Impairments in seeing and smell; dizziness; proprioceptive function; tingling; central pain		
Digestive system functions	Impaired ingestion; constipation; reduced weight maintenance		
Genitourinary and reproductive functions	Impaired urination and sexual functions		
Skin and related structures functions	Impairments in sweating and sebum production and sensations related to the skin		

Physical capacity assessment should focus on the mobility of cervical, thoracic and proximal joints, length of muscles, and strength of major muscle groups. For the assessment of mobility, the examination of joint ROM and general flexibility is important. Musculoskeletal impairments tend to begin proximally, affecting the contractile and non-contractile tissue length and flexibility first of the spine and girdle and then of the more distal musculature. As the disease progresses, PD patients are likely to develop a reduction in joint ranges, specifically for hip and knee extension, dorsiflexion, spine and neck extension, axial rotation and lateral flexion of the spine, shoulder flexion, and elbow extension. Using a digital or standard goniometer, the therapist can document the passive range of motion of the larger joints and spinal inclinometers, cervical range of motion instruments, and cervical or head-mounted laser for the spine. In clinical settings, spinal mobility can also be examined using a series of functional movements, in seated or standing positions, like looking behind and turning the neck sideways or upwards.

Generally, the muscle groups of the spine and limbs become shortened and limit extension throughout these structures. Passive straight leg raise with the pelvis and opposite thigh stabilized can be used as an easier method to check the hamstring length. Testing the tightness of hip flexors, specifically the iliopsoas and hip adductors, and plantar flexors, can be incorporated into the routine assessment. However, care has to be taken not to create undue stretch and pain while examining the muscle tightness.

The deconditioning effect, the reduced physical activity, and the hypertonicity predominantly in the flexors of the spine and limbs cause weakness of muscles, specifically the anti-gravity muscles, contributing to the flexed posture in the middle and advanced stages of PD. Traditional manual muscle testing can be used for the assessment of muscle strength and can be performed using the Medical Research Council (MRC) grading system (Table 4.4). Alternatively, handheld and isokinetic dynamometry can be used for the quantitative measurement of muscle strength, including peak force, torque output, power, and angle of maximal force.

Table 4.4 Medical Research Council Grades for Muscle Power

MRC grade	Description
0	No contraction
1	Flicker or trace of contraction
2	Active movement, with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

Grades 4−, 4, and 4+, may be used to indicate movement against slight, moderate, and strong resistance, respectively.

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As the disease progresses, the movements are slowed (bradykinesia), then movements decrease in range and amplitude (hypokinesia), and in the later stage, movements are characterized by start hesitations and are eventually akinetic. Stopwatch and use of grooved pegboards can help quantify the bradykinesia due to slowness and hesitancy of movement.

The clinical assessment of rigidity in PD is largely qualitative. In the early stage of the disease, the distribution of rigidity is often asymmetrical and can vary particularly during the course of the day, with the medication timing and stress. The level of resistance offered during the passive movement and the Range of Motion (ROM) available can provide information about the severity of rigidity. The grades of rigidity (Box 4.1) can also be documented in the motor examination component of the Unified Parkinson's Disease Rating Scale (UPDRS). In addition to the grading of rigidity mentioned in the UPDRS, Columbia University Rating Scale (CURS) can be used to grade the rigidity. The grade of rigidity is judged by passively moving the major joints with PD patients, preferably in sitting position for upper and lower limbs and neck. The Webster rating scale is another clinical assessment tool to grade the degree of rigidity in PD patient's limbs and neck.

Box 4.1 Grades of Rigidity

Grades	Features
0	Rigidity absent
1	Rigidity slight or detectable only when activated by mirror or other movements
2	Mild to moderate rigidity
3	Marked rigidity, but full range of motion easily achieved
4	Severe rigidity, range of motion achieved with difficulty

Camptocormia, scoliosis, and antecollis are a few of the spinal deformities seen in PD. Assessment should focus on posture, both static and dynamic, in lying, sitting, standing, and while walking. It should also cover the ability to actively correct posture and manipulate objects while sitting and standing. Posture grids, plumb lines, and software analysis of the 2D photographic images or captured videos can be used for the same purpose.

Patients with Pisa syndrome are more likely to have considerable asymmetry in symptoms, increased muscular activity, back pain, postural and balance dysfunction, and a poorer Quality of Life (QOL) when compared with PD patients without Pisa syndrome. The prevalence of Pisa syndrome among PD is approximately 9%. The tendency to lean worsens while walking. The onset of Pisa syndrome symptoms can be acute (within a few days or weeks), subacute (over a few months), and chronic (insidious). In the early stage, the majority of PD patients are less likely to be aware of the lateral trunk deviation. In the advanced stage, the patients often experience debilitating pain, dyspnea, unsteadiness, and falls while walking. It is important to emphasize that the terms "scoliosis" and "Pisa syndrome" are not

synonyms. The former cannot be improved by passive movement or supine positioning and is characterized by radiological evidence of a structural curve with axial vertebral rotation that persists when the effect of gravity has been eliminated. The pathomechanism(s) underlying Pisa syndrome is not fully understood. Central and peripheral are the two hypotheses proposed for the same. The central hypothesis considers Pisa syndrome as a consequence of the basal ganglia dysfunction along with altered sensorimotor integration and possibly exacerbation by dopaminergic treatment. Whereas, the peripheral hypothesis considers alteration of the musculoskeletal system as the possible mechanism for the development of the same. The perception of verticality is affected in PD patients and abnormal perception, together with dysfunction of central graviceptive pathways can alter the sensorimotor integration essential for postural stability. Research has also suggested that the asymmetric functioning of the basal ganglia circuit could be the primary cause of the development of Pisa syndrome.

The syndrome is also reported in other conditions including dementia, Parkinsonism, normal-pressure hydrocephalus, Alzheimer's disease, Lewy body disease, and subdural hematoma. It can be a result of exposure to antipsychotic, dopaminergic, and antidepressant drugs. Though there is no consensus on the diagnostic criteria for the Pisa syndrome, the diagnosis is based on clinical examination and accurate measurement of lateral deviation of trunk, using a standard goniometer. Early recognition and either withdrawal of offending medication or revision of drug regimen can prevent veering of this syndrome toward the chronic irreversible variant.

Though not always as troublesome as bradykinesia and rigidity, the tremors may often interfere with routine functional activities. The location and the severity of resting and/or action tremor and to what extent the functional skills like drinking, feeding, dressing, and writing are affected, need to be noted. Due to impairments in motor planning and programming, PD patients may have difficulty to perform multitask (cognitive and motor) and dissociated movements in the middle and advanced stages. The assessment should include observation of the patient's ability to perform dissociation movements of trunk and limbs, dual and multitasks (a combination of cognitive and/or motor), sequential activity, continuous movements without visual guidance, and spontaneous switching from one to another activity.

Though PD is considered a motor disorder, during the progression of the disease, non-motor issues like cognitive deterioration and digestive and genitourinary dysfunctions also emerge. Memory impairments, attention deficits, language issues, and abstract reasoning, problem-solving, and judgment issues are some of the important cognitive deficits that need evaluation. Speed of information processing, attention, and concentration are particularly important when bradyphrenia (inattentiveness and delayed response) is suspected. For the abovementioned, cognitive function scales like Mini-mental State Examination (MMSE) scale or Montreal Cognitive Assessment (MoCA) can be used as a screening tool. In addition to cognitive dysfunction, the presence of depressive symptoms like sadness, apathy, insomnia, anorexia, inactivity, dependency, difficulty concentrating, and impaired memory can be worrisome. The geriatric depression scale or the Beck depression inventory can be used as an instrument to self-report it.

The presence of sway during quiet stance, both medial-lateral and anterior-posterior planes, indicates a poor postural control. Normal subjects typically respond to small shifts of the center of mass using ankle strategy and for larger shifts, by hip and stepping strategies. PD patients, when destabilized, typically respond with postural strategies involving the hip joints or stepping, more than ankle joints. PD patients, especially in the early stage, may not demonstrate balance impairments in a steady stance with a normal base of support or self-initiated movements. However, when competing attentional demands are instituted like talking while balancing or mental calculations while balancing, may demonstrate instability. The common and often used balance measurement tools like the Berg Balance Scale (BBS), the Functional Reach Test (FRT), the Timed Up and Go (TUG) test and the Dynamic Gait Index (DGI) have been reliable and sensitive in the examination of functional balance in PD patients. The retropulsion test or the pull test will evaluate the patient's response to an unexpected, quick, and firm backward pull on the shoulder. Taking multiple steps (three or more) to regain balance as a response to the pull test clinically suggests impairment of balance. Usually, the measurement values of balance using the abovementioned scales or tests are quite stable during the "on" phase of the medication and are less reliable and more fluctuating during the "off" period.

Gait examination should cover unobstructed walking on a level surface, start time or gait initiation, speed of walking, stride length, cadence, stability, variability, and safety. Increased difficulty in walking is also experienced in response to varying attentional demands and dual-task interference. Changes in gait parameters like speed, stride length, and cadence can be observed while simultaneously performing a secondary cognitive task or motor task. A 10-m walk test can help to determine the speed, average stride, and cadence of the patient. Force plates, body markers, 3D videographic and computerized equipment, and software analysis can be used for sophisticated kinetic analysis of the gait. Gait should be examined for kinematic or qualitative changes, including reductions in the hip, knee, and ankle motions that result in a short-stepped, shuffling (festinating) gait pattern. Postural abnormalities that contribute to the development of a festinating gait pattern should also be documented (i.e., flexed, stooped posture).

Several gait impairments, including rhythm control, gait symmetry, bilateral coordination of gait, dynamic postural control, and step scaling, have been associated with Freezing of Gait (FOG) with PD. FOG is a stronger predictor of activity limitation than gait hypokinesia. In the early and middle stages of the disease, the freezing phenomenon is often difficult to assess due to its less predictable nature. In these stages, freezing episodes are less likely to occur during the "on" time and are usually levodopa sensitive; however, during the advanced stage, the episodes are often seen during "on" and "off" times. The Freezing of Gait Questionnaire (FOG-Q), a self-administered measurement tool, is appropriate for assessing the FOG in clinical practice. There is a strong association between the FOG and the risk of falls. The patient or the family members/caregivers may use a fall risk diary to record the fall events. The events recorded should cover information such as activity at the

time of the fall, direction and method of landing, number and frequency of near-misses, type of footwear used, fatigue, the timing of medication, food intake, and other possible intrinsic or extrinsic risk factors for fall. To gauge the fear of falling, a short version of the full 16 item Falls Efficacy Scale-International (FES-I) is recommended in clinical practice.

Clinical examination also should address the problems with autonomic dysfunction such as drooling (salivation) or sweating, greasy or oily skin, and abnormalities in thermoregulation. Excessive sweating and flushing during the "on" state may have an association with dyskinesia. Signs and symptoms of orthostatic hypotension like lightheadedness or dizziness, confusion, blurring of vision, fatigue, nausea, and syncope need to be documented, if any, after standing up. A drop of 20 mm Hg in the systolic blood pressure or a drop of 10 mm Hg in the diastolic blood pressure within 2–5 min of standing up is diagnostic of the condition.

Sedentary nature with decreased physical activity and impaired cardiorespiratory function may reduce the endurance of PD patients. In the advanced stage of the PD, respiratory dysfunction can be a major concern as the presence of upper airway obstruction and co-existing chronic obstructive pulmonary disease can predispose to pulmonary complications and even death. Careful observation of rib cage compliance, mobility of the chest wall, breathing patterns, and monitoring of ventilator-derived parameters like Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 s (FEV1), maximal expiratory flow, total lung capacity, and residual volume and objective measures including measurement of chest cage mobility and respiratory rate, are to be incorporated when required. In addition to the above, PD patients are known as "silent aspirators" with weak cough reflex. The presence of tongue tremor, hesitancy in initiating swallowing, long time to finish a meal, difficulty in bolus formation, coughing when eating or drinking, change of voice while feeding, abnormal gag reflex, and reduced pharyngeal mobility are certain clinical observatory findings of swallowing dysfunction which may predispose to aspirations.

Individuals with minimal symptoms of PD (1 and 2 of the Hoehn and Yahr scale) may demonstrate aerobic exercise capacities similar to healthy adults. Individuals with more advanced disease (2.5 and above of Hoehn and Yahr scale) may demonstrate a greater variability and lower aerobic capacities compared to healthy adults. To determine the endurance capacity and the walking velocity, 6 or 12-min walk test can be used. While determining the endurance capacity, the vital parameters like heart rate, respiratory rate, and blood pressure, and exertional symptoms like pallor, dyspnea, dizziness, and fatigue need to be documented. A 2 or 3-min walk test is a sensitive and feasible tool to evaluate the walking endurance of advanced PD patients, while Borg's rating of perceived exertion (RPE) is a feasible scale for perceived exertion. The Borg's scale allows participants to subjectively rate their level of exertion during exercise or exercise testing, starting with a minimal score of 6 which means "no feeling of exertion" and ending with a maximum score of 20 which means "very, very hard." Table 4.5 provides instances of tasks performed by a normal healthy adult below 65 years of age for different Borg's RPE scores.

Table 4.5 Examples of activities or tasks with respect to Borg's rating of perceived exertion scores

Borg's RPE score	Description about the exertion	Examples of tasks performed by a normal healthy adult below 65 years age
6	No exertion	Listening to the radio, reading a book, or watching a movie
7–8	Very, very light exertion	Rolling the sleeves of a shirt or tying the shoe laces
9–10	Very light exertion	Daily chores like laying dinnerware on a dining table or folding clothes
11–12	Fairly light exertion	Walking through the grocery store or similar activity that requires some effort but not enough to speed up the breathing
13–14	Somewhat hard	Brisk walking or other activities that require moderate effort and speed your heart rate and breathing but do not make you out of breath
15–16	Hard	Running, swimming, bicycling, or other activities that take vigorous effort and get the heart pounding and make breathing very fast
17–18	Very hard	Highest level of activity one can sustain
19–20	Extremely hard, maximum exertion	A finishing kick in a race or other burst of activity that you cannot maintain for long

4.2.5.2 Staging of Parkinson's Disease

Not all PD patients experience all the symptoms of the disease. Even in typically progressing PD, the patients may experience the symptoms in quite the same order but not necessarily at the same intensity. The condition does not progress in a straight line and it is often difficult to pin down the exact progression, pace, and severity of the disease. PD rating scales are a means of assessing the symptoms and providing information about the course of the condition and/or QOL. Such scales may also help to evaluate the management strategies and can be useful for clinicians, research scholars, patients themselves, and caregivers. In the past, based on the degree of disability or progression of the disease or the person's ability to perform daily activities in terms of speed and independence, several PD rating scales have been introduced. The Webster rating scale, the Hoehn and Yahr scale, and the Schwab and England ADL scale are some of them.

The Hoehn and Yahr scale, widely used in clinical settings and research, originally described in 1967 by Margaret Hoehn and Melvin Yahr, describes the symptoms progression and the level of disability. The original scale had stages 1 through 5 and has been modified (Box 4.2) with the addition of 1.5 and 2.5 to the former stages. In the recent past, this rating scale has been complemented by the UPDRS which covers both motor and non-motor symptoms. The UPDRS scale was introduced in 1987 and it combines the elements of other Parkinson's rating scales to produce a comprehensive and flexible tool to monitor the disease course and the degree of disability. Box 4.3 provides parts and constituents of UPDRS.

Box 4.2 Modified Hoehn and Yahr Scale

Stage 0: No signs of disease
Stage 1.0: Symptoms are very mild; unilateral involvement only
Stage 1.5: Unilateral and axial involvement
Stage 2: Bilateral involvement without impairment of balance
Stage 2.5: Mild bilateral disease with recovery on pull test
Stage 3: Mild to moderate bilateral disease; some postural instability; physically independent
Stage 4: Severe disability; still able to walk or stand unassisted
Stage 5: Wheelchair-bound or bedridden unless aided

Box 4.3 Unified Parkinson's Disease Rating Scale: Parts and Constituents

Part I: Evaluation of Intellectual Function, Mood, and Behavior:	**Part II: Self-evaluation of Activities of Daily Living:**
Forgetfulness, disorientation in time and space; vivid dreaming; hallucinations; delusions and paranoia; depressed mood; anxious mood; apathy; features of dopamine dysregulation syndrome; nighttime sleep problems; daytime sleepiness; pain and other sensations; urinary problems; constipation problems; lightheadedness on standing; fatigue	Speech; salivation and drooling; chewing and swallowing; handwriting; cutting food and handling utensils; dressing; hygiene; trouble doing hobbies and other activities; tremor impact on activities; getting in and out of bed; walking, balance, and falling; freezing
Part III: Motor Examination:	**Part IV: Evaluation of Motor Complications:**
Speech–volume, diction; reduced facial expression; rigidity; finger tapping; slow hand movements; rapid alternating movements of hands; toe tapping; leg agility; rising from chair; posture-stooped; gait; postural stability; body bradykinesia; tremor at rest	Dyskinesia including time spent with dyskinesia, functional impact of dyskinesia, and painful off-state dystonia; motor fluctuations, including time spent in the off state, functional impact of fluctuations, and complexity of motor fluctuations

4.2.5.3 Exercises and Training Interventions for Parkinson's Disease

The gradual deterioration of functional capacity is a well-known feature of PD. Advancement in recent drug therapy has considerably improved functional expectancy. Current evidence suggests that medical management, in conjunction with physiotherapy, can potentially delay the onset of physical disabilities. Despite the direct effects of the disease, the combination of pharmacological intervention with physiotherapy may provide some psychological well-being for the PD patient.

To maximize functional ability and minimize the complications, a variety of interventions including pharmacological intervention, physiotherapy, semi- and/or unsupervised home exercise program taught by the therapist and performed by the patient under the supervision of family members, environmental modification for the home setting, and supportive counseling are required. Early intervention may play a crucial role in averting or minimizing the musculoskeletal impairments, which PD patients are bound to develop. Physiotherapy should focus on the improvement of motor performance, functional capacity, and activity participation.

Application of Principles of Learning in Training Impairments in motor planning and programing and the absence of internal cueing mechanisms cause gradual deterioration and loss of both formal and informal learned skills. It is essential to emphasize to the patient that the conscious incorporation of appropriate movements is required for skill "reacquisition" and permanent gains are possible only if the patient "relearns" the desired maneuver. Learning, "a change in the internal state of the individual causing a relatively permanent improvement in performance which occurs as a result of practice or experience," is a process that is not directly observable, but can be implied from the behavior or performance of the participating subject. The cognitive (associated with intellectual activities), the affective (emotional control and moral judgments) and the psychomotor (deals with the acquisition of motor or perceptual-motor skills) domains are the three domains of learning and all of them are interdependent.

In PD, the principles of psychomotor learning are applicable for re-mastering or relearning the skills which are faulty or missing. The cognitive, the fixation, and the autonomous are the three phases through which learning occurs in the psychomotor learning domain. The cognitive phase is the initial, more theoretical phase of learning, where the learner focuses on understanding the principles, details, and components of the skill. In this phase, the learner tries to process the information in an attempt to cognitively understand the requirements and parameters of the motor skill. Keen observation and attention are required from the patient to process the information and the physiotherapist should pay attention to key parts of the skill and may need to demonstrate the movement for a better mental picture. In the fixation or associative phase, fundamentally a practical phase, the learner will be attempting to translate declarative knowledge into procedural knowledge until skill acquisition is made. This phase is characterized by conscious performance, smaller gains in performance, lesser verbal information, corrections, disjointed movement, and a longer time to complete the task. This is the phase where learners attempt to reduce the number of errors from feedback. Both knowledge of result (externally generated feedback either by a therapist or trainer) and knowledge of performance (ongoing feedback about the performance, usually from a monitoring device or a videotape replay) play a central role in motor skill acquisition. For realistic motor learning, sufficient and frequent practice with appropriate feedback is critical. "Practice does not make the act perfect but makes it permanent," implies the role of the correct method of practicing for optimal learning. Generally, during the early stage of skill

acquisition, a considerable amount of feedback in the form of knowledge of result or knowledge of performance is required; however, the frequency of feedback reduces as the learner masters the skill.

In the autonomous phase, the final phase of skill acquisition, the motor performance becomes largely automatic, cognitive processing demands are minimal and the learner is capable of attending other information (information related to other skills or tasks). In this phase, the learner is able to implement the skill at the highest level, with the least conscious effort like a habit. Interestingly, due to progressive impairments in motor planning and programming, even in the autonomous phase, the patients can typically lose the ability to carry out the learned or relearned motor skills. The breakdown of skills can be visible in the form of small errors during motor performance. For instance, several sessions or days after re-mastering the gait, the therapist may notice a slight stooping of the trunk that was not there earlier. Such errors will grow in numbers and size with repetition and time. Therefore, to salvage the deterioration in the acquired skills, the early detection of such errors is crucial. The therapist or the caregiver who is being sensitized about the same should watch for such movement errors and intervene in a timely manner. To eliminate the newly detected errors, the patient should pass through all the phases of psychomotor learning, beginning with the cognitive phase. Mental practice, another psychomotor learning concept, consists of cognitive rehearsal in the absence of overt physical practice. It can be used as an adjunct to augment relearning of motor skills. However, mental practice may not be an appropriate strategy for patients in the advanced stage when cognitive capabilities are diminishing.

In the early and middle stages of PD, externally generated cues and performance through practice can be helpful in improving their capacity to learn complex movements and sequences. The absence of internally generated cues makes the learning of complex movements and sequences difficult. For learning complex movement sequences, the sequence has to be broken into simple component parts and each part has to be practiced separately and in sequential order with the help of appropriate visual, auditory, and somatosensory cues. Lengthy movement sequences and random practice order have to be avoided and block practice of the component parts has to be encouraged to reduce the effects of contextual interference. The home setting should be the preferred treatment setting if performing complex sequential tasks and movements are problematic in other settings. However, in the advanced stage with pronounced cognitive deficits, such training is less likely to be successful. PD patients may often demonstrate motor learning deficits like slower learning rates, increased dependence on context-specific learning, and lack of generalizability. Repetitive practice and use of structured instructional sets while training have shown improvement in movement speed and consistency even in the advanced stage of disease or with cognitive deficits. To develop procedural skills, practicing with a large number of repetitions is crucial. Providing instruction to focus the attention on the desired movement and an environment that minimizes distraction and competing attentional demands may help learn the skill more efficiently before attempts are made for a different environmental context.

Kinesiological and Mechanical Perspectives for Parkinson's Disease Training Posture and movements are constrained by kinesiological imperatives and mechanics laws. From a kinesiologic and mechanical viewpoint, postural changes cause compensatory postural strategies and alterations in muscular activities. In PD patients, the vertebral segment mobility is typically reduced or lost throughout the cervical, thoracic and lumbar spine. Analysis of posture and movements based on the mechanical and kinesiologic perspectives may reveal movement constraints imposed by the disease, mainly, the lack of segmental mobility of the spine (spinal rotation, lateral flexion, and spinal extension). Alterations like the above may force PD patients to depend on compensatory strategies like long sitting from supine, instead of a roll to one side for sitting. The analysis may also reveal the overuse of rectus abdominis, instead of the abdominal obliques for roll to one side to sit. Therefore, therapy should focus on segmental mobility activities, specifically emphasizing segmental rotation patterns (i.e., isolated upper and lower trunk rotations). Rhythmic initiation using diagonal patterns of Proprioceptive Neuromuscular Facilitation (PNF), on a therapeutic mat and encouraging the PD patients to practice rolling on a firm to soft surfaces may benefit the patient to improve bed mobility skills and trunk flexibility.

The developmental sequence of postural control (a natural and predictable movement progression a normal infant follows during early life to develop abilities to roll, crawl, kneel, stand, and walk) progresses from kinesiologic simple to kinesiologic complex movements. Lower developmental postures within the neurodevelopmental sequence provide the necessary strength, stability, and coordination required for more challenging postures. Such postures minimize the risk of falls and maximize movement efficiency. With the perspectives mentioned above, initial treatment including management of rigidity and encouragement of mobility or flexibility should preferably commence in a fully supported supine position, even if the patient is ambulant and somewhat independent.

Strategies to Reduce Rigidity Generally, rigidity tends to be more in the axial and proximal muscle groups and may predispose for postural and musculoskeletal alteration, which may be unilateral in the earlier stage. Slow rocking can be used to promote the generalized relaxation of skeletal muscles secondary to rigidity. Rocking the patients while being comfortably seated on the rocking chair can induce relaxation and sleep. Both vestibular and somatosensory stimulation associated with rocking may exert a synchronizing action in the thalamocortical networks that reinforces endogenous sleep rhythms. Neurophysiological research supports the notion that vestibular stimulation associated with rocking is related to the relaxation of muscles. The known functional interrelationships of vestibular structures with the cerebellum and reticular activating system and vestibular structures to autonomic centers can explain the association between vestibular stimulation and relaxation and sleep. Prior to flexibility exercises, posture correction and functional training, upper and lower trunk rotation and counter-rotation (rotating the upper trunk to one side while the lower trunk is rotated in the other side) movements or diagonal patterns of PNF like slow, rhythmic, chopping movement performed in the

supine position can be helpful to promote relaxation. The rhythmic initiation technique of PNF, moving progressively through passive, active-assisted, and active movements, may reduce the rigidity. Relaxed diaphragmatic breathing exercises and incorporation of bilateral symmetrical diagonal PNF patterns into relaxed breathing exercises can promote relaxation and improve chest expansion. To achieve relaxation, PD patients can also try music therapy and meditation techniques either in lying or well-supported seated positions.

Flexibility and Stretching Exercises Flexibility exercises improve ROM and physical function. The flexibility exercise should go hand in hand with the relaxation techniques for rigidity. If the patients have achieved adequate relaxation, the therapist will be able to feel the segmental mobility at the vertebral, girdle, and proximal joints when passive flexibility exercise is attempted. Flexibility exercises should progress through passive to active-assisted to active. A gentle warm-up exercise or use of hot fomentation can be useful to minimize the possibility of capsular or ligament injury while performing stretching or flexibility exercises of those tight joints. To counter the thoracic kyphosis and promote upper trunk extension, bilateral symmetrical diagonal PNF patterns can be utilized.

Positional stretching techniques can be useful to stretch tight muscles and soft tissues. In late-stage PD, patients are likely to develop severe tightness and flexion contractures of the trunk and limb muscles. Prone-lying for 20–30 min on a daily basis can be beneficial to provide positional stretch for the trunk and limbs flexors. For tight hip flexors, if prone lying is uncomfortable, then high-kneeling with hip in extension or hook-lying bridging can be used as an alternative strategy to stretch the same. Unilateral PNF pattern that emphasizes hip and knee extension can counter the typical flexed, adducted position of the lower extremities. In the advanced stage, following the onset of cardiorespiratory impairments and the development of significant postural deformity, the patient may not be able to tolerate the prone position. For such patients, mechanical stretching can be achieved through the use of a tilt table.

Vigorous and quick passive ROM exercises need to be avoided due to the chance of soft tissue injury. Such stretches may create apprehension in PD patients and also stimulate pain receptors to cause rebound muscle contraction, further worsening the muscle hypertonus. If the bones are osteoporotic, vigorous stretches and quick passive movements may predispose to fractures among elderly PD patients.

Strategies to Reduce Tremor In the ambulatory stage (up to the fourth stage of Hoehn and Yahr scale), resting and/or action tremor, bradykinesia and hypokinesia, rigidity, postural alterations, gait abnormalities, and loss of facial expression can be present, but in varying severity. In some PD patients, tremors may predominate over bradykinesia, rigidity, and postural alterations and make gross motor skills like bed mobility, transitions, and gait, and fine motor skills like dressing and handwriting difficult or impossible to perform. Pharmacological and non-pharmacological treatment strategies are available when tremors are more disturbing than bradykinesia and rigidity. Some of the non-pharmacological strategies for tackling resting trem-

ors include maintenance and stabilization of the arms (proximal joints) as close as to the body when carrying out activities and avoiding multitasking like shaving, brushing, or cooking while standing. Managing stress, anxiety, frustration, and fatigue that are known contributors to resting tremors and the use of adaptive equipment like powered toothbrush, adaptive utensils, and weighted cutlery may help to reduce the tremors.

Training to Improve Posture Following flexibility exercises and stretching exercises, the focus of training should be on improving the posture of the patient. Often the correction of posture further improves the mobility of the joints, specifically the rotation of the spine. In addition to altering the balance and gait, the typical stooped posture seen in IPD also causes swallowing difficulty, weak and soft speech, reduced strength of postural muscles, and pain in the joints. Verbal instructions like "chin-tuck" to reduce the forward head posture, "sit tall" to improve the thoracic kyphosis, and "bring the shoulder blades closer" to improve scapular retraction and minimize the rounding of the shoulders, can be incorporated for posture correction. Such exercises need to be performed regularly with a 1–2 min hold. Posture correction exercises should progress from a seated position with back support to without back support. To correct the posture in standing, the therapist can advise the IPD patient to stand against the wall or stand with the back facing the wall. Meanwhile, verbal instructions like "stand as close as possible to the wall," "tuck the chin," "allow the back of the head, the trunk and the buttocks to be in contact with the wall," and "knees straight and feet as close as to the wall," can help to improve the posture. Regular and repeated practice of such posture correction exercises will help the patient to consciously correct the posture until the posture correction becomes a habit. In addition to the above, the use of mirror, cueing, and biofeedback can complement or be an alternative to the standard methods of posture correction. Exercises with an elastic band can also be incorporated as a method of strengthening the muscles and for improving the posture.

For those PD patients with the Pisa syndrome, to minimize the potential for permanent postural deformities, early rehabilitation, emphasizing stretching exercises for the external oblique and paraspinal muscles, is strongly recommended. An individualized program consisting of proprioceptive and tactile stimulation, combined with stretching, flexibility exercise, cueing, and postural re-education, can be a beneficial, safe and feasible strategy to overcome the postural abnormality. Functional strengthening exercises, especially the extensor muscles, bridging exercises, trunk flexion and rotation exercises, in addition to gait training and balance training, can also be attempted. Investigators have reported that the use of Kinesio® taping for the trunk muscles as an adjunct treatment had no long-lasting beneficial effect compared to conventional therapy. The exercise regimen (overcorrection strategy) used for correcting the listing tendency in stroke patients, as seen in Pusher's syndrome (mentioned in Chap. 3—"Stroke") can be attempted as an alternate strategy to minimize the postural abnormality due to Pisa syndrome.

Strength Training Strategies The PD patients who demonstrate poor posture and functional deficits like the inability to get out of a chair and difficulty performing overhead activities using the upper limb, secondary to the trunk and proximal limb muscle weakness may benefit from strength training. Reduced physical activity, a consequence of aging, and reduced basal ganglia output leading to lower levels of cortical and spinal motor activation are the possible reasons for muscle weakness. Studies on strength training among PD patients have shown improvement in muscle force, bradykinesia, and QOL. Strength training, specifically, progressive resistance strength training, based on the progressive overload principle using free weights, elastic bands, manual resistance, or strength-training equipment, can be used in the clinical or home setting for strengthening the muscles. For each muscle group, a set of 10–12 repetitions and 14–15 rate of perceived excursion on the Borg's scale can be recommended for most of the PD patients. Bridging exercise performed on a stable and unstable surface (gym ball), strengthens the hip extensors and the spinal extensors. Functional training exercises can be an alternative to improve muscle strength. Unlike progressive resistance strength training, functional training exercises are multi-joint and multiple planar movements consisting of compound exercises requiring more than one muscle group to work together. Functional training exercises typically mimic everyday movement patterns like squats and pull-ups. Incorporating rotational components into functional training, in addition to developing muscle strength, will improve flexibility. The disease process and aging are known to cause deconditioning effects. General conditioning programs like aerobic exercises, strengthening exercises and functional training may retard the process of deconditioning effects and maintain the optimal level of physical function.

Training Sit to Stand Transitions PD patients typically sit with a stiff trunk with a posterior pelvic tilt. Exercises designed to improve pelvic mobility and tilt (including anterior and posterior tilt movements and side-side pelvic tilt) along with the extension of the spine can be practiced while sitting on a therapeutic gym ball and later on a firm, stable surface like a therapeutic mat. Exercises in sitting should include weight shifts emphasizing trunk rotations and reach outs. For sit-to-stand transition training, the PD patient will be instructed to scoot his or her trunk forward to the edge of the therapeutic mat. Following this, the patient will be instructed to place the feet on the floor right under the knees at a hip-width apart. Verbal instructions like "sit tall" are to be given to encourage the patient to sit with an erect spine. While maintaining the spine in extension, the patient should be asked to flex the trunk over the hips. Guidance and cues can be used for encouraging the flexion of the trunk over the hips. Assistance and support may be given to perform the standing-up by extending the lower limbs, followed by an extension of the spine. Premature extension of the spine during this training process will make the standing-up difficult or faulty. Proprioceptive training on a firm surface, including static and dynamic partial squats, weight shifts and single-limb stance using stall bars or

manual assistance of the therapist and strengthening exercises for lower extremity muscles can help the PD patients to smoothly execute sit-to-stand transitions. The sit-to-stand transitions should be progressively practiced from a standard height chair to a lower chair. For those patients where safety is a concern while standing, the use of a harness system or chair with armrests can be an alternative. Once even weight-bearing through lower extremities is possible, activities like weight shifts and rotational movements of the trunk should be introduced in standing.

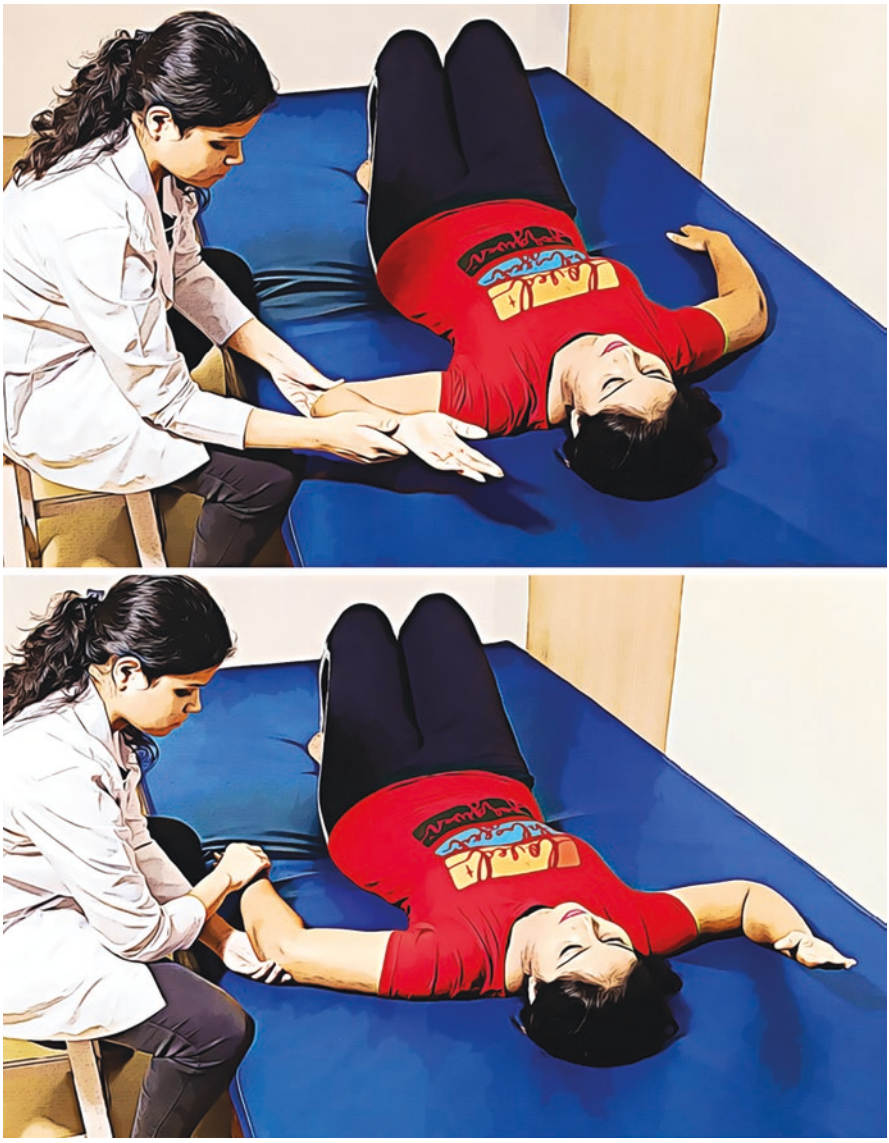
Role of Dissociation Movements In addition to the bradykinesia and deficits in motor learning, PD patients typically exhibit undue difficulties in the execution of simultaneous or sequential complex movements of two or more joints of the limbs. Many goal-directed motor acts require such a series of movements, sequential and/or simultaneous, at different joints and of different limbs. Even PD patients can have motor issues like the inability to switch from one motor act to another or execute two different motor acts simultaneously with opposite limbs. The motor planning and programming impairments due to the involvement of the basal ganglia circuitry are the plausible cause for this. Training the patients to perform simultaneous symmetrical movements of limbs (Fig. 4.8) progressing toward simultaneous asymmetric movements [alternating or dissociating in nature] (Fig. 4.9) and adding more complexity by incorporating both upper and lower limbs [simultaneous dissociation movements of shoulder girdle with respect to pelvic girdle] (Figs. 4.10 and 4.11) may improve the ability of the PD patient to execute two different motor acts simultaneously with opposite limbs. In the beginning, the therapist may need to demonstrate the movement and may need to guide and assist the patient in performing such simultaneous alternating movements. For the training program mentioned above, the use of the therapeutic mat with the patient in a supine position is desirable before more advanced developmental postures are attempted. Like the training given for transitions and balance and gait, to master dissociations or alternative movements, the use of relevant instructions and adequate repetitive practice is critical.

Balance and Gait Training Strategies In PD, automatic motor behaviors or adjustment movements like arm swing while walking or weight shifts while standing that accompany voluntary movements and righting and balance are either impaired or faulty. Typically, balance issues are likely to develop within 5 years after the onset of initial symptoms and within another 5 years, recurrent falls will be a major concern. Balance training should be an integral part of the exercise training program, especially when the PD patients' assessment reveals balance impairments. PD patients can take advantage of the balance training programs designed to improve balance among the healthy elderly provided their specific problems are taken into consideration, i.e., prior to the commencement of balance training, it is essential to address issues such as rigidity, flexibility, and postural abnormalities. Balance training should be given in both the seated and standing positions. The training should focus on controlling the center of mass and improving the limits of stability. While maintaining a near-normal or normal postural alignment, the patient should be encouraged to expand the limits of stability. The use of verbal, tactile, or proprioceptive cues and appropriate and well-timed feedback can encourage the

Animated photographs of model and therapist with permission

Fig. 4.8 An illustration of the symmetrical movements of the upper limbs

patient to achieve balance without postural disturbances and falls. Balance training should progress from stable to an unstable surface, static to dynamic positions of limbs or trunk, seated activities to activities in standing, a calm environment to a busy environment, open eyes to closed eyes, and a larger base of support to a small base of support like progression through quadruped, kneeling, half-kneeling and



Animated photograph of model and therapist with permission

Fig. 4.9 An illustration of the asymmetrical movements of the upper limbs

standing. Verbal instructions like “stand tall” or “do not bend” and use of a mirror(s) for postural feedback are often encouraging. During balance training, encourage the PD patients to initiate and execute movement as fast as they can. Self-initiated displacements are preferred over perturbations given by the therapist or the caregivers as the latter can create more apprehension and worsening of rigidity and postural

Animated photograph of model and therapist with permission

Fig. 4.10 An illustration of the asymmetrical movements of the upper and lower limbs

Animated photograph of model and therapist with permission

Fig. 4.11 An illustration of the asymmetrical movements of the upper and lower limbs and the neck

stiffness. For PD patients with recurrent episodes of falls, finding safe ways of standing, identifying key activities causing falls, environmental adaptations, strategies to reduce the fear of falling, and teaching cognitive strategies to avoid or manage situations that can challenge balance are certain recommendations to minimize the episodes of falls.

The basal ganglia circuitries play a key role in running complex motor sequences that make up skilled, largely automatic, movements like gait. For the lower extremity, gait is a complex and sequential automatic activity. Gait training goals focus on reducing primary gait impairments (including reduced velocity, reduced step and stride length, lack of trunk rotation, lack of arm swing, festinating pattern, lack of normal heel-toe pattern, and the tendency to stoop while walking) and improving the PD patient's ability to safely perform functional mobility and avoid falls while walking. Verbal instructions such as "walk fast," "big step," "do not bend," and "swing arms" can enhance velocity, step length, posture, and arm swing. Practicing marching in place and progressing toward an exaggerated high stepping walking may improve the ground clearance if the patient has a tendency to walk with short steps, poor ground clearance, and shuffling.

Role of Cues in Gait Training In basal ganglia disorders like PD, a key motor problem about sequential movements is the deficiency of automatic maintenance of appropriate scale and timing. Festinating or shuffling gait in PD is arrhythmic, small in amplitude, and variable, and often exhibits reduced automaticity of movement and increased attention directed toward the gait. Cueing is a well-established compensation strategy for improving locomotion when internal cueing mechanisms are defective. Unlike clues (hints), cues are prompts and can be auditory, visual, tactile, verbal, or others. Normally, basal ganglia, pre-supplementary motor cortex, and dorsolateral prefrontal cortex use internal cues to initiate self-generated movements.

The external cues can compensate for errors in the internal cueing mechanisms. External cues, either visual or auditory, appear to facilitate movement by utilizing the different regions of the brain, including the premotor cortex and cerebellum. Unlike the internal cueing responsible for learned movements that are more automatic, external cueing bypasses the defective basal ganglia and uses cortical circuitry with heightened attention for generating movements. Therapeutic cueing uses external temporal or spatial parameters to facilitate movement initiation and continuation. Cues given in the early stages of PD tend to improve or maintain quality and avoid deconditioning, while in the later stages help to compensate for the reduction of automaticity. The benefits of cueing are dependent on the type (auditory, visual or other) and the parameters (spatial or temporal) used. For instance, cues that focus on step amplitude primarily affect step size, whereas cues that focus on step rhythm primarily affect the number of steps. Similarly, auditory cues tend to have a greater influence on the temporal components such as cadence and stride synchronization, than on the spatial components of gait.

Since attention plays a critical role in the efficacy of external cueing, the presence of medication instability and disease fluctuations in the advanced stage of PD, and cognitive impairments can often make cueing ineffective. In the early and middle stages of PD, external cues are found to be effective in triggering sequential movements. Visual cues, including floor markings and dynamic stimuli like strobe lights or laser light from the cane or walker, have shown significant improvement both in stride length and velocity and reduced tendency for freezing, but not in cadence. Rhythmic auditory stimulation, including metronome beats or steady beats

from a musical device, has shown an improvement in gait speed, cadence, and stride synchronization. Auditory cues should be consistent and rhythmical and the speed of the beat for auditory cueing should preferably be set 25% faster than the patient's preferred pace. With regard to visuospatial cues, transverse visuospatial cues (across the gait path) may be more beneficial than parallel cues (alongside the gait path) in improving gait velocity, stride length, and stance time. The use of floor markers or footprints on the floor can be strategies to improve foot placement. Existing literature suggests that visual cues are relatively better than rhythmic auditory cues, despite the extra attention required for the former. However, literature also reveals that PD patients in the home environment prefer auditory cues over visual cues.

Management during the Advancing Stage In the advancing stage of disease (3–4 of Hoehn and Yahr scale) many of the PD patients will experience freezing episodes. The episodes are sudden, short, and transient and primarily occur while attempting to initiate a walk, navigate through obstacles or negotiate narrow spaces or curbs. The freezing episodes are often triggered by emotional stress, environmental constraints, and dual tasking and may lead to reduced physical activity levels and functional capacity. Defective perceptual judgment, impaired bilateral coordination of gait, and impaired integration of vision with spatial memory can be a few of the contributing factors for the freezing phenomenon. Studies have noted reduced step length, increased cadence, and premature timing of anterior tibialis muscle and gastrocnemius muscle prior to the episodes. Physiotherapy can be helpful to reduce or overcome freezing episodes. The strategies that can prevent or overcome freezing may include the use of metronome, change of direction by stepping sideways or backward, weight shifting before attempting a step, trying to march in place, verbalizing "1-2-3-go" and then stepping forward, initiating a movement of any body part like swinging an arm and stepping over an imaginary line in front. Often, the strobe lights from the cane or the walker can work as a visual cue, and verbal cues like "heel down" or "stand tall" may help the patient overcome the freezing episodes.

Patient and Family Members Education and Advanced Stage Management Regarding symptom progression and advancement of disability, PD is more obscure compared to other progressive neurological conditions like motor neuron disease and Alzheimer's disease. This often necessitates the need to educate the patient and family members about the disease, the medications, dosage, and their side effects, and the preventive strategies to avoid or minimize the complications. The therapist should teach the family members or caregivers the basic and safe techniques of lifting, maneuvering, and transferring the patient and exercises like bridging and pelvic rolling that can assist in the day-to-day care of the patients. Both the patient and the family members should be taught the strategies that can circumvent the movement abnormalities to solve functional problems. The family members should also be encouraged to augment the patient's motivation for performing functional activities.

In the advanced phase (fifth of Hoehn Yahr stage) of the disease, pharmacotherapy becomes less effective and the complications are likely to increase both in magnitude and frequency. Symptoms, including dyskinesia, are more pronounced during the end of dose failure and drug on-off phases making patients functionally dependent. The therapist should keep track of the on-off phases and should provide therapy before the beneficial effects of medications wear off. Preferably the therapy should begin 45 min to 1-h post-medication when the patient is at his or her best. Intensive therapy to improve the facial and oromotor functions, breathing exercises and chest manipulations for lung dysfunction, frequent changes of bed position to prevent decubitus ulcers are certain treatment objectives during the late stage.

4.2.5.4 Alternate Therapies

Aquatic Physiotherapy or Hydrotherapy Aquatic physiotherapy or hydrotherapy can be an alternative to land-based exercise training protocols. The aquatic environment can promote significant therapeutic results such as a reduction in muscle tone, improvement in postural stability, and increment in functional mobility. The warm water used in the aquatic pool may have a potential therapeutic effect on rigidity. Current literature also states that both land and water-based protocols are useful for improving balance. Supervision during aquatic exercise is a must as there is a potential hazard for slips, falls, and drowning. Close monitoring of hygiene and infection control is required to minimize the possibility of infection. Dehydration can be yet another important concern for older adults. The patients should be encouraged to drink 250 ml of water 1 h prior to the pool therapy.

Treadmill Training A considerable amount of literature is available with regard to the use of treadmill in neurorehabilitation. Current literature shows a greater improvement in motor performance compared with conventional therapy for stride length, gait speed, and symptoms. The locomotion training on the treadmill also has a positive effect on balance and QOL. “With the treadmill, there is no getting around it; the patient must match his/her pace to the treadmill.” The treadmill acts as an external cue by setting the walking pattern and reinforcing the neuronal circuits (provides an external rhythm that compensates for the defective internal rhythm). Increasing the walking demand and gait speed is believed to cause adaptive neural plasticity which improves gait parameters. Training on the treadmill can be progressed by reducing the body weight support given through the harness, increasing the treadmill speed, reducing the physical assistance, and increasing the duration of time on the treadmill. The use of a safety harness is mandatory for PD patients with balance deficits or FOG during treadmill training. For such patients, if the purpose of treadmill training is to improve endurance but not the gait, arm or leg cycle ergometer is a better and safer alternative.

Lee Silverman Voice Treatment (LSVT) 'Big' Program Also known as "training big" program, the LSVT consists of a therapist-guided high intensity, large amplitude, multiple repetitions, and whole-body exercises, based on the concept that repetitive high-amplitude movements yield greater improvements in motor performance. This exercise is believed to have a neuroprotective effect and is performed 1 h per session, four sessions per week, and studies have shown improvement in the UPDRS motor scores and the gait parameters of 1–3 Hoehn and Yahr scale stage PD patients.

In addition to the above, several alternate therapies, including high-intensity indoor cycling, dance therapy, music therapy, tandem cycling, and Nordic walking, have been studied and have shown promising results for PD patients in the alleviation of symptoms and gait parameters improvement. However, further details regarding those alternative therapies are beyond the scope of this chapter.

4.3 Other Extrapyramidal Disorders

4.3.1 Wilson's Disease (Hepatolenticular Degeneration or Westphal–Strömpell Pseudosclerosis)

Wilson's disease is an inherited metabolic progressive lenticular degenerative disorder associated with liver cirrhosis. Wilson's disease is transmitted as an autosomal recessive trait and the prevalence is about 1–2 per 100,000 of the general population. Siblings of the affected one have a 25% chance of developing the disease. The classical description of the disease was published by Samuel Alexander Kinnier Wilson, a British neurologist, in the year 1912. Wilson entitled his article "Progressive lenticular degeneration: a familial nervous disease associated with cirrhosis of the liver," in which he gave a detailed description of four cases. Prior to the detailed description by Wilson, in 1883, Adolph Strümpell, a German neurologist, and in 1898, Karl Friedrich Otto Westphal, a German psychiatrist under the title named "pseudosclerosis" had given details about the same; however, none of the descriptions, including Wilson's, addressed the association of liver cirrhosis with lenticular degeneration. About a decade before Wilson presented his monograph, in 1902, Bernhard Kayser, a German ophthalmologist, first described a rusty-brown ring, a corneal abnormality and within a year, Bruno Fleischer, another German ophthalmologist, related it to hepatic degeneration. In 1913, A. Rumpel demonstrated the increased copper content within the liver of Wilson's disease patient. The clinical and histopathologic studies by H. C. Hall and W. Spielmeyer (1920–1921) clearly established the association of lenticular degeneration with liver cirrhosis. The same year, H. C. Hall proposed genetic inheritance as an autosomal recessive pattern and in 1953, A. G. Bearn confirmed it by genetic ratio analysis calculation. It was A.J. Glazebrook in 1945 and John Cumings in 1948, in their independent studies, linked copper accumulation with the basal ganglia and

hepatic pathology. In 1952, Herbert Scheinberg and David Gitlin demonstrated a low level of serum ceruloplasmin in this disorder.

4.3.1.1 Etiology, Neuropathology, and Pathogenesis

Mutation of a gene on chromosome 13q14.3, which encodes a copper transporting ATPase, is the genetic cause of the disease. A reduced rate of incorporation of copper into ceruloplasmin and a reduction in biliary excretion of copper are the two copper metabolism dysfunctions caused by the genetic defect. Abnormal accumulation of copper in the liver and the brain is caused by defective cellular transport and failure of the liver to excrete copper into bile. The hepatic cellular damage and neuronal cell damage secondary to the abnormal accumulation of copper cause the hepatic and neurological manifestations of the disease.

Pathological findings include enlargement of the ventricles, flattening of the convexity of the head of the caudate nucleus, and lesions in the middle zone of the putamen. The caudate nucleus and putamen appear atrophic, shrunken, and crumbly and in untreated patients, cavitation can also be seen. Rarely the cavitations can be seen in the thalamus, subthalamic nuclei, dentate nuclei, and cerebral cortex. In some cases, multifocal demyelination affecting the cerebral white matter with no primary evidence of inflammatory pathology can also be seen. The myelin staining reveals central pontine myelinosis. Pontine myelinolysis can be the most striking pathology in the brainstem. In general, the pathological involvement of the lentiform nucleus is more prominent than that of the caudate nucleus and pallidum.

4.3.1.2 Neurological Manifestations and Investigation Findings

Generally, the onset of the disease is in the second or third decade of life. Acute or chronic hepatitis and splenomegaly are the first expressions of the disease due to the deposition of copper (Cu) in the liver. The patient can have a history of several attacks of symptomatic jaundice or may present with neurological signs and symptoms in the absence of jaundice. Usually, the neurological manifestations are gradual and insidious, but sometimes with intermittent acute deteriorations or rapid progression. Less frequently, the early manifestations of this disorder can be psychiatric, renal, hematological, or musculoskeletal. The early neurologic manifestations are most often extrapyramidal, consisting of tremors in the limbs and head and bradykinesia. Tremors can be resting and/or postural in nature and when the limbs are outstretched, they may display a coarse, “wing-beating” tremor. Bradykinesia of tongue, lips, pharynx, larynx, and jaw results in dysarthria, dysphagia, and hoarseness. Saccadic movements of the eyes are often slow and have the limitation of upward gaze. Often the patients may display choreiform movements or dystonic posturing of the limbs with flexed or stooped posture, dystonic gait, and sometimes with stridor. During the progression of the disorder, elements of cerebellar ataxia and intention tremor of variable degree may get added to the existing symptoms.

Cerebellar features may include cerebellar ataxic gait, scanned and/or staccato speech, limb ataxia, intention tremor, and titubation of the head. Kayser–Fleischer (KF) rings (rusty brown or golden brown ring visible around the corneo-scleral junction/limbus) in the eyes become more evident as the neurologic manifestation of the disease evolves. In addition to the development and advancement of motor impairments, in the later stage, intellectual functions will also progressively decline. Timely diagnosis and treatment are of utmost importance and if delayed, the disease may progress and the patient can become extremely rigid, dystonic, mute, immobile, and mentally slowed.

The presence of reduced serum ceruloplasmin level within the blood, low serum copper, increased excretion of copper through urine, high copper content in hepatic cells after liver biopsy are certain laboratory findings. The liver function test generally is abnormal. The Computed tomography (CT) scan may reveal atrophic changes in the basal ganglia, cortical and cerebellar regions, associated with dilatation of lateral ventricles and third ventricle and widening of cerebral and cerebellar sulci. T1 weighted Magnetic Resonance Imaging (MRI) scans can demonstrate hyperintensity in lentiform nuclei and mesencephalic regions (Fig. 4.12). T2 weighted scan may demonstrate hyperintensity which typically involves the putamen, globus pallidus, caudate nucleus, and the ventrolateral part of the thalamus. The axial T2 weighted scan at the level of the brainstem may reveal the “double panda sign” (a face of a panda at the midbrain level and a cub of a panda at the pons level).

4.3.1.3 Medical and Surgical Management

If the condition is diagnosed before the onset of the neurologic manifestations, the use of copper (Cu) chelating agents and reduction of dietary intake of Cu can reverse the changes caused by the disease. D-penicillamine remains the principal Cu chelating agent and to prevent anemia, pyridoxine should be given daily. Trientine or ammonium tetrathiomolybdate can be a substitute for D-penicillamine. The use of medication has to be a lifetime to avoid disastrous clinical deterioration as there are no pharmacological interventions that can reverse or stop the defective copper metabolism. The patient should abstain from copper-rich foods, including liver, cocoa, chocolate, mushrooms, and shellfish. With the decoppering therapy, the KF rings usually disappear and the liver function test may return to normal. Early diagnosis and prompt use decoppering agents may prevent or reverse otherwise permanent and fatal clinical manifestations of this disease. Even for those patients with neurological signs and symptoms, the commencement of decoppering therapy may reduce the neurologic manifestations. For those patients with severe liver damage, liver transplantation will cure the underlying metabolic defect and may reverse some of the clinical manifestations.

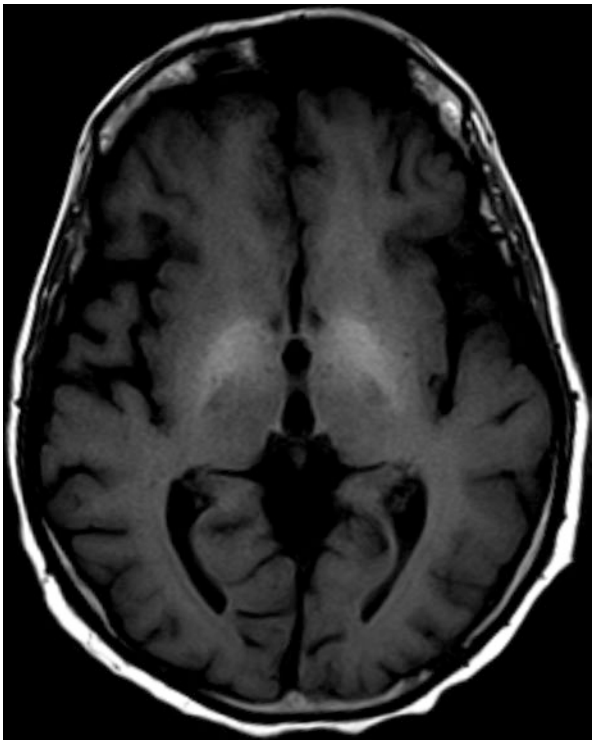


Fig. 4.12 MR axial T1 weighted scan demonstrating hyperintensity typically involves putamen, globus pallidus, caudate nucleus, ventrolateral part of the thalamus consistent with Wilson's disease or metabolic disease

4.3.1.4 Physiotherapy Management

Dystonia, incoordination, tremors, balance issues, and gait abnormalities are the common manifestations of this disorder and the therapy can play an effective role in the treatment of Wilson's disease. Positional stretch and gentle passive stretching or flexibility exercises can be helpful to retard or prevent the progression of contractures secondary to dystonia. For acute or dynamic contractures, serial cast application can be helpful to regain range and flexibility. In cases where cerebellar movement abnormalities are more worrisome for the patient, exercises to minimize dysmetria of limbs or trunk can be given. Isometric exercises, along with slow reversal hold technique progressing toward rhythmic stabilization exercises given for the neck and trunk musculature may reduce the titubation movements and truncal ataxia.

The balance training used for PD or cerebellar (discussed in Chap. 5—Cerebellar Dysfunction) patients can be of benefit to improve balance reactions and limits of stability of patients with Wilson's disease. For patients with mobility and safety issues, walking aids and environmental modifications of the home settings can be

helpful. If general weakness and fatigue and/or aches and pains of muscles are the concerns, either due to the extrapyramidal or liver dysfunction, exercises to improve the patient's functional capacities, energy conservation techniques, and pacing strategies to manage fatigue and pain management using electrotherapeutic modalities or thermal agents can be the preferences.

4.3.2 Multiple System Atrophy

Multiple System Atrophy (MSA) is an adult-onset, often fatal neurodegenerative disorder. It was originally described under different diagnostic terms, namely Olivopontocerebellar atrophy, Striatonigral degeneration, and Shy–Drager syndrome. In 1969, J.G. Graham and D.R. Oppenheimer, both British neurologists, first introduced the term MSA to combine these clinicopathological disorders. Based on the predominant clinical features, the MSA is categorized into the Parkinsonian (MSA-P), cerebellar (MSA-C), and autonomic (MSA-A) subtypes. It is estimated that the prevalence is approximately 3–5 cases per 100,000 general population. MSA is a disease of middle-age life and usually, the onset is between 40 and 70 years. With regard to gender preference, males have a higher predisposition over females and the survival is approximately 6–10 years from the initial onset of symptoms.

4.3.2.1 Etiology, Neuropathology, and Pathogenesis

Though the etiology of MSA is largely unknown, genetic causes including COQ2 mutation, SHC2 copy number loss, and unidentified autosomal dominant or recessive gene mutations and environmental causes including organic solvents, pesticides, plastic monomers, and metal dust may act as causative factors for the neuropathogenesis of this disorder. Pathologically, along with the characteristic glial cytoplasmic inclusions, the disease is characterized by a variable extent of neuronal loss and gliosis in the striatum, cerebellum and middle cerebellar peduncles, substantia nigra, locus ceruleus, pontine nuclei, inferior olivary nuclei, and intermediolateral columns and Onuf's nucleus of the spinal cord. In addition to the above, the disorder is also characterized by the presence of α-synuclein within the glial cytoplasmic inclusions. In MSA-P, the neuronal loss and gliosis are more prominent in the substantia nigra and striatum, whereas in MSA-C, the loss is more in the cerebellar cortex, middle cerebellar peduncle, and brainstem.

4.3.2.2 Neurological Manifestation and Investigation Findings

This disorder is known for its marked clinical variability. The presence of one or more features of autonomic symptoms, including orthostatic hypertension, bladder and bowel incontinence, and sexual dysfunctions, dysphonia and/or stridor,

slowness of movement, rigidity, Babinski sign, and cerebellar ataxia, and less possibility of resting tremor are some of the common features of MSA. Usually, the disease begins with asymmetric striatonigral-parkinsonian features or with prominent autonomic manifestations often associated with disabling orthostatic hypotension. The cerebellar features may rarely dominate the initial stages of the disease. In MSA-P, the extrapyramidal features can be more severe than PD and within 5 years, the patient can be wheelchair-bound or bed-confined. The relative symmetry of the signs and symptoms, rapid course, poor response to levodopa, absence or minimal amount of tremor, presence of prominent autonomic dysfunction, and the less obvious eye movement abnormalities make it easier to distinguish MSA from PD. Imaging techniques may frequently reveal cerebellar and pontine atrophy, aiding the diagnosis of the condition. The T2-weighted MRI will show putaminal hypodensity and increased deposition of iron. The PET scan may disclose impaired glucose metabolism in the striatum and the frontal cortex.

4.3.2.3 Medical Management

No definite management exists as there are no pharmaceutical interventions available to halt or reverse the progression of MSA. For MSA-P, symptoms may alleviate with levodopa, dopamine agonists, or anticholinergics medications. Administration of botulinum toxin can be helpful to reduce dystonia of the hand, foot, or trunk. If autonomic dysfunctions are worrisome, fludrocortisone or desmopressin for nocturnal polyuria, antimuscarinic agents or anticholinergic medication for bladder dysfunction, fluids and laxatives for constipation, tracheostomy for stridor and intracavernosal papaverine for impotency can be administered. Clonazepam, GABApentin, or buspirone can be used for myoclonus or action tremor.

4.3.2.4 Physiotherapy Management

Due to the complex nature of MSA, the best treatment is gained from a multidisciplinary team approach. The team, a group of health and social care professionals, may include a neurologist, family physician, nurse, physiotherapist, speech therapist, clinical psychologist, and dietician. Physiotherapy treatment objectives and means vary for each subtype and stage of the disease. Adequate knowledge about the disease helps the therapists choose the appropriate clinical skills to manage this condition. The goals of therapy should be realistic and appropriate and the therapy must be integrated into daily living.

The motor symptoms of MSA-P (rigidity, bradykinesia, tremor, and poor balance) are similar to those observed in typical PD and for the same reason, the therapist can use the same strategies and treatment for handling the abovementioned issues. Physiotherapy can often be challenging when postural hypotension is accompanied by fatigue. Graduated programs of activity, avoiding prolonged stance and activity, and pacing can minimize fatigue over time. Use of 30° elevation of the

head-end of the bed while sleeping, progressive acclimatization using a tilt table, use of abdominal binders, and compressive stockings for the lower limbs can be strategies to manage orthostatic hypotension. Recommending a sufficient amount of fluid (up to 2–3 l/day) intake, especially before exercise, avoiding warm environments and activities that may elicit the Valsalva maneuver will possibly minimize the postural hypotension. If festination and FOG are issues for MSA-P patients, the use of cues (discussed earlier) can be beneficial. Cognitive strategies can be encouraged right from the early stage of the disease as they will act as adjuncts for safe ambulation and for overcoming freezing. Since gait ataxia, truncal ataxia, and dysmetria of the limbs are certain common features of cerebellar disorders, strategies and training programs for cerebellar dysfunction can be extrapolated for the management of MSA-C.

4.3.3 Progressive Supranuclear Palsy

In 1964, John Steele, Clifford Richardson, and Jerzy Olszewski, in their seminal report of nine cases with autopsy confirmation, first described Progressive Supranuclear Palsy (PSP). Following their pioneer work, this disease was known as the Steele–Richardson–Olszewski syndrome. As originally described, PSP is characterized by progressive supranuclear ophthalmoplegia, gait disturbances, postural instability, dysarthria, dysphagia, rigidity, and frontal cognitive disturbance. Under atypical Parkinsonism, PSP is considered to be the most common degenerative form. The prevalence of PSP is approximately 6 per 100,000 population. The average age of onset of this disease is around 60 years. Other than age, there are no proven risk factors for the development of PSP. Males have a higher predisposition for this disease (8:1). In most cases, the disease progression is relatively rapid and relentless and most PSP patients will become dependent on care within 3–4 years after the onset of symptoms and the patient usually succumbs to death within 6–12 years after the onset of symptoms.

4.3.3.1 Etiology, Neuropathology, and Pathogenesis

Most cases of PSP appear to be sporadic. Similarly, there is no conclusive evidence that exposure to industrial wastes, specifically phosphate and chromate ore, has any association with PSP. The PSP belongs to the family of disorders known as “tauopathies” (a group of neurodegenerative diseases having abnormal aggregation of tau protein in neurofibrillary or gliofibrillary tangles within the brain). It is the abnormalities in the protein tau (a microtubule-associated protein, the main component of the intracellular filamentous inclusions) that lead to damage in the cortical, subcortical, cerebellar, and brainstem areas of the brain. Histologic examination reveals neuronal loss, gliosis, and the presence of tau-positive filamentous inclusions in specific anatomic areas involving astrocytes, oligodendrocytes, and neurons. The tau cytoplasmic inclusions in surviving neurons, known as globose neurofibrillary

tangles, are classical findings in PSP. Autopsy examination has disclosed a bilateral loss of neurons and gliosis in the superior colliculus, periaqueductal gray matter, tegmentum of the brainstem, substantia nigra, oculomotor nucleus, red nucleus, globus pallidus, and subthalamic nucleus and to some extent in the dentate nucleus and vestibular nuclei. Hypopigmentation of the substantia nigra and locus ceruleus and enlargement of the third ventricle are the additional findings. Neurochemical studies have shown the degeneration of dopaminergic neurons in the striatum, cholinergic and GABA interneurons, and efferent neurons in the basal ganglia and the brainstem.

4.3.3.2 Neurological Manifestation and Investigation Findings

Richardson phenotype or syndrome is the most common and "classic" phenotype of PSP. Broad-based gait with short step length, shuffling steps, gait freezing and lurching with postural instability, and frequent falls are the early and usual presentations of this phenotype. Supranuclear ophthalmoparesis (largely downward gaze palsy) is the hallmark of PSP. Initially, the patients may show slowing of vertical saccades, but with time (3–7 years), all voluntary eye movements will be completely lost, beginning with the vertical gaze and then the horizontal ones (ophthalmoplegia). However, if the patient is instructed to fix the eyes on a target and the head is turned, the clinician can observe the full range of eye movements, proving the supranuclear, nonparalytic character of the gaze palsy.

Dysarthria, dysphagia, pseudobulbar palsy, rigidity, frontal cognitive abnormalities, and sleep disturbances are additional common clinical features. Retracted upper eyelids, wide-opened eyes, and reduced blink with a stare impart an expression of "perpetual surprise" for PSP patients. In some PSP cases, blepharospasm and involuntary eye closure can be prominent issues. Rigidity in PSP patients will be more apparent in the axial musculature than in the limb musculature, specifically the neck and upper trunk. PSP patients, while walking, tend to hold their trunk and lower limbs extended, arms slightly abducted and on pull test for postural instability, classically stagger backward uncontrollably. The rigidity of the trunk musculature and postural instability may cause the PSP patient to consistently lean and fall backward (retropulsion). Resting tremor is an unusual finding in PSP and the patients will not have limb ataxia, Romberg sign, or postural tremor. In a few cases, Babinski signs can be present. Impaired abstract thinking, reduced verbal fluency, and motor perseveration (continuation or recurrence of a motor activity with difficulty to switch between actions; a sign of frontal lobe lesion) are the cognitive dysfunctions seen in PSP. Apathy, disinhibition, irritability, anxiety, impulsivity, and dysphoria are certain common behavioral symptoms of PSP. In the later stage, some degree of dementia can be present in PSP patients and may complain about sleep disturbances and increased urinary frequency and urgency. In the advanced stage, the patients become anarthric, immobile, fully dependent, and wheelchair-bound or bedridden.

Currently, the diagnosis of PSP is based upon clinical features. A gradually progressive disorder, with the age of onset 40 years or above, progressive upward or downward gaze supranuclear palsy and prominent postural instability with falls,

with no evidence of symptoms or features suggestive of other diseases like hallucinations, history of encephalitis, cortical sensory deficits, cortical dementia and dysautonomia help in the clinical diagnosis of the condition. Neuroimaging studies will demonstrate generalized atrophy of the brainstem, particularly involving the midbrain. MRI of the brain certainly will reveal the classical "penguin silhouette" or "hummingbird" sign (Fig. 4.13), a sign resulting from the prominent midbrain atrophy with the relative preservation of pons. On axial imaging, MRI can reveal the "Mickey Mouse" sign (Fig. 4.14) due to the atrophy of the dorsal mesencephalon (superior colliculi, red nuclei). As the earliest sign of PSP, the PET scan may reveal reduced glucose metabolism in the midbrain.

4.3.3.3 Medical Management

Like MSA or IPD, no therapeutic intervention can alter the natural course of this disease. Medications that provide significant symptomatic benefits, as seen in IPD, have less beneficial effects in PSP. Poor or short-lived response to levodopa therapy is the usual finding in PSP and can help clinicians to distinguish PSP from IPD. Zolpidem, a GABAergic agonist of benzodiazepine receptors, has been reported to ameliorate rigidity and akinesia. Focal dystonia and drooling issues can be managed by the local administration of botulinum toxin. In some cases of PSP, amantadine can provide a transient therapeutic benefit for dyskinesia and drooling issues. Davunetide, a neuroprotective agent, is assumed to maintain microtubule function, reduce tau phosphorylation, and inhibit apoptosis in PSP. The concerns like dysphagia and dysarthria, to a certain extent, can be managed by health professionals like dietitians and speech therapists.

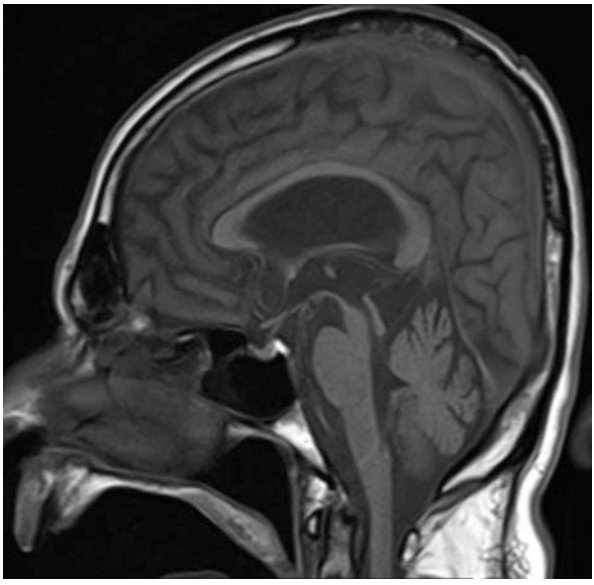


Fig. 4.13 MRI T1 sagittal of the brain revealing the "penguin silhouette" or "hummingbird" sign, a sign resulting from the prominent midbrain atrophy with relative preservation of pons consistent with the diagnosis of PSP

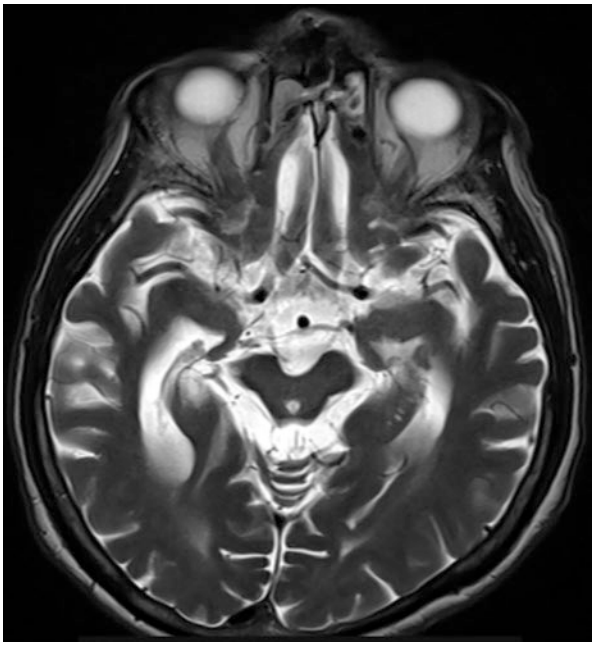


Fig. 4.14 MRI T2 axial imaging revealing the "Mickey Mouse" sign due to the atrophy of the dorsal mesencephalon (superior colliculi, red nuclei) consistent with the diagnosis of PSP

4.3.3.4 Physiotherapy Management

Though the neuropathological findings are somewhat different between IPD and PSP, evidence is available, citing the commonality of certain clinical features among them. From a logical point of view, the treatment modalities proven to be successful in improving motor deficits in PD can be relevant and useful for PSP patients also. Studies have shown that exercise programs focusing on gait, balance, and prevention of falls are feasible and safe for PSP patients. Certain studies reported that aerobic, intensive, motor-cognitive, goal-directed exercises along with treadmill training with or without robotic assistance had improved the spatio-temporal parameters of gait (including cadence, step/stride length, and gait velocity) in addition to the reduction of fall risk and improvement of balance. Due to the high cost and the low benefit-cost ratio, for many of the clinical settings and community-dwelling PSP or PD patients, the robotic-assisted treadmill or treadmill with the bodyweight supporting system may not be a viable option. In addition to treadmill training with or without robotic assistance, several other approaches, including balance training with a tilt board, resistive or isokinetic strength training exercises, and coordination exercises, have been used for gait training.

The treatment strategies like exercises to improve aerobic capacity, balance training for improving balance, sit-to-stand transitions for safe and effective transitions, flexibility exercises to improve mobility of the joints and encourage segmental rotations and movements, motor-cognitive exercises, and use of cueing for improving gait and functional capacities may have beneficial effects as seen in

IPD. Strategies to overcome freezing and prevent falls can also be trained to minimize freezing episodes and the potential for injury, respectively. For patients with ophthalmoplegia, head and neck movements, specifically emphasizing downward and sideways movements, have to be encouraged to see the surroundings and the floor while walking to avoid obstacles.

If retropulsion and tendency to keep the spine in extension are quite prominent in PSP patients, activities like bridging and spinal extension exercises are not advisable. In such cases, strengthening the abdominals (rectus abdominis and external and internal oblique muscles) in supine and encouraging forward reaches and oblique forward reaches while seated can reduce the tendency of retropulsion. Most of the patients have a tendency to prematurely straighten the spine during the sit-to-stand transition, predisposing then to fall backward. Practicing sit-to-stand transition, specifically with trunk bend forward over the hips may reduce the tendency to fall backward until the postural controls are severely affected. Even activities like reaching and picking up objects from the floor while seated on a therapeutic mat (low height) may encourage the patient to bend the trunk adequately for sit-to-stand transitions. During gait training, unlike for IPD patients, instructions to bend the trunk upon the hips and to keep the knees slightly bend may minimize the possibility of leaning backward or falling backward.

4.3.4 Huntington's Disease

A concise description of a syndrome, likely to be Huntington's disease, was first given by Charles Oscar Waters, an American physician, in 1841. In 1872, George Huntington, another American physician, first gave a complete description of Huntington's disease (HD), including the salient clinical features of the disease, the pattern of transmission, and the dismal prognosis. "Huntington's chorea" is a cardinal sign of the disease. Though chorea is an important clinical sign, not all HD patients may present with chorea. Movement abnormalities, affective disturbance, and cognitive impairment are the clinical triad of this disorder. The disorder is autosomal dominant inherited, with a 50% chance of the affected individual's offspring developing the disease during their adult stage. Though genetic studies can identify the pre-symptomatic subjects, no treatment can prevent or ameliorate progressive neurodegeneration. In most countries, the prevalence rate is approximately 4–10 per 100,000 population. The HD is reported from all parts of the world, but it is more common in certain regions like Scotland and Venezuela. Though the disease is rare, the burden the disease can put on the patients, the family members and their offspring is indescribable.

4.3.4.1 Etiology, Neuropathology, and Pathogenesis

Mutation of the gene known as "huntingtin gene" located on the short arm of chromosome "4" is the cause for HD. The gene product of the huntingtin gene is a protein called "huntingtin." Although the exact function of the huntingtin protein is

unclear, this protein may be involved in chemical signaling, transporting materials, binding to other proteins, and protecting the cell from apoptosis. The mutation involves a DNA segment known as a CAG (cytosine, adenine, and guanine) trinucleotide repeat in the huntingtin gene. Abnormal expansion of a repeating CAG triplet series leads to an increase in the size of the CAG segment, causing the production of an abnormally long version of the huntingtin protein. The elongated huntingtin protein disintegrates into smaller toxic fragments that bind together and accumulate in neurons (specifically in GABAergic medium spiny neurons) within the striatum and certain parts of the cortex. The early disruption of GABAergic medium spiny neurons in the indirect pathway of basal ganglia, normally presumed to inhibit movements, results in choreiform movements. The disruption of medium spiny neurons in the direct pathway is a plausible explanation of the rigidity and bradykinesias in the later stage of the disease.

Pathologically, HD is characterized by marked atrophy and prominent neuronal cell loss in the bilateral basal ganglia, especially the striatum. The atrophy is associated with a widening of the anterior horns of the lateral ventricles. The anterior parts of the putamen and caudate are more affected than the posterior parts. In addition to the above, neuronal cell loss also occurs in other regions of the brain, including the third, fifth, and sixth layers of the cerebral cortex, especially the frontal and temporal regions, with a certain amount of gliosis. Studies revealed that the neuronal cell loss in HD patients made their brains smaller and lighter as compared to the age-matched controls. The degree of neuropathological changes is generally milder in older onset cases compared to younger onset cases; however, the relationship between the neuropathological changes and the clinical features is unreliable. Histological examination of the striatum reveals the involvement of the smaller neurons before the larger ones, early loss of dendrites of the small spiny neurons, and replacement of the lost cells by fibrous astrocytes. PET studies have revealed impaired glucose metabolism of the striatum prior to the visible atrophy of the same.

4.3.4.2 Neurological Manifestation and Investigation Findings

The disorder usually starts between 35 and 55 years of age. If the age of onset is below 20 years, then those cases are of “juvenile” form or phenotype, which accounts for about 5% of the total cases. Unlike the adult form of HD, during the initial onset of symptoms, the juvenile form tends to present with bradykinesia and rigidity over chorea. The initial manifestation of symptoms can be either neurological or psychiatric or both. The neurological manifestations of the disease are usually insidious in nature. Rarely, HD patients may present with frank neurological and/or psychiatric features. Often, the initial manifestations can be non-specific, including complaints like feeling depressed, forgetful, or clumsy. In general, chorea is the early movement abnormality manifestation seen among HD patients. In the early stage, chorea may be barely perceptible and first noticeable in the hands and face. As it evolves, the severity of chorea may vary from mild restlessness to an intermittent exaggeration of gestures, fidgeting movements, unstable dance-like gait, to a

continuous flow of disabling violent movements. These choreiform movements cannot be voluntarily suppressed and stress and anxiety can worsen them. The chorea of HD causes a lurching, stumbling, stuttering, dipping, and bobbing gait with steps forward, backward, or to one side. The gait of HD is complex and dance-like, with the velocity of gait slow, stance time varied from step to step, the base of support wide, and excessive trunk sway while stepping. Dystonic posturing of the hip or knee, either in flexion or extension, can punctuate the ongoing stepping motion. Despite the apparent gait deviation, balance and equilibrium are usually preserved till late-stage and surprisingly the frequency of falls is also less.

In HD, the eye movements are usually slow from the early stage, characterized by difficulty in initiating saccades and broken pursuits. Unlike PD, the frequency of blinking of the eyes is increased in HD. The unwanted darting movements of the tongue may constantly interrupt when the voluntary protrusion of the tongue is attempted. Speech may reveal a marked variation in rate, loudness, and timing, distortion of vowels, harshness of voice, sudden stoppages of speech, and poor coordination with breathing (hyperkinetic dysarthria). The speech abnormalities are indeed the result of choreiform movements affecting the coordination of phonatory and respiratory muscles. Typically, as time passes, the chorea will cease to progress and get overshadowed by dystonia, rigidity, and bradykinesia. Eventually, a progressive increase in rigidity and bradykinesia causes immobility, postural instability, and inability to walk.

Spasticity, brisk deep tendon reflexes, and extensor plantar responses are unlikely in HD. Impairment of movement can affect the laryngeal and respiratory muscles leading to dysphonia. Dysphagia and cachexia are common issues during the middle and late stages of the disease and often become the usual cause of choking and aspiration of oral contents leading to death. Patients may develop insomnia at night and somnolence during the day. The bowel and bladder incontinence common during the late stage may be a consequence of dementia than a specific neurological cause.

In HD patients, managing the cognitive and affective impairments can be more challenging than managing the movement disorder. Patients themselves may be unaware or unconcerned about the cognitive, affective, and motor changes and often it is the family members that bring them to medical attention. Approximately one-third of HD patients report psychiatric and behavioral symptoms as the early manifestation of the disease. Depression is a very common problem and may precede the onset of a variety of neurological dysfunctions. A low threshold for anger, a minimal provocation to react, fear, temper tantrums, irritability, apathy, and sleep disturbances are some of the psychological and behavioral problems seen. Due to the high rates of depression and fear of the disease, the risk of suicide is more common in HD than in other neurological disorders. Mania and hypomania are less commonly seen when compared to depression. Though psychosis is rare, it can be a common feature among early-onset HD, often difficult to treat. Some HD patients may display obsessive-compulsive features or altered sexual behavior. Behavioral and psychiatric manifestations may predate the onset of overt HD by as long as a decade,

reflecting early pathological changes in the non-motor areas of the striatum. The general decline in intellectual functions during the course of the disease is a cognitive impairment manifestation of the disease. The dementia of HD (subcortical dementia) presents with cognitive slowing, memory retrieval deficits, attentional difficulties, and executive dysfunction in the absence of aphasia and apraxia. Right from the early stage, the cognitive impairments, specifically the executive dysfunction, may render HD patients unable to work, drive and manage family finances. Even though there is dysarthria and slowness of thinking, many patients may retain the ability to comprehend until the late stage of the disorder.

In the adult phenotype with early-onset, affective disturbances are more often the initial complaints and precede the motor and cognitive impairments by years. In the middle years, the motor and cognitive impairments tend to appear nearly at the same age, whereas, in older age onset, choreiform features are more often the initial problems. The mean survival is 17 years from the onset of the symptoms. Due to the diverse and complex problems associated with HD, a multidisciplinary team (including neurologist, nurse, psychiatrist, physiotherapist, occupational therapist, dietician, speech therapist, and social worker) approach is essential to manage such patients.

In HD, the radiological investigation may reveal atrophy of the caudate nucleus (mainly the head), putamen, and frontal lobes. As the disease progresses, diffuse cortical, thalamic and limbic atrophy may also appear. In addition to the above, T2 weighted MRI images may reveal hyperintense or hypointense signal changes typically in the putamen. The T2 hyperintense signal change is usually attributed to marked neuronal loss and gliosis. In the early stage of disease, when the chorea is more prominent, the T2 weighted MRI images may not reveal any change in signal intensity.

4.3.4.3 Medical Management

With a typical clinical picture and a confirmed family history, the diagnosis of HD is often straightforward. Rarely, vague family history, inaccurate parental information, denial, and obfuscation can make the diagnosis difficult. No pharmacological treatment can reverse, undo or halt the neurodegenerative process. Since the condition is characterized by changes in motor, affective and cognitive symptoms, the medications are likely to evolve over the course of the disease. Currently, the treatment for HD is supportive and/or symptomatic in nature. Tetrabenazine and deutetrabenazine can be used to suppress the chorea associated with HD. Ironically, medications to alleviate the chorea may make bradykinesia, dystonia, and apathy worse. Haloperidol, fluphenazine, risperidone, olanzapine, and quetiapine can be used as antipsychotic drugs. However, these antipsychotic drugs may worsen chorea, dystonia, and drowsiness. Citalopram, escitalopram, fluoxetine, and sertraline are antidepressants, and divalproex, carbamazepine, and lamotrigine can be the mood-stabilizing drugs for HD.

4.3.4.4 Physiotherapy Management

Developing a standard or conventional treatment program for HD patients is difficult due to the heterogeneity of clinical signs and symptoms among patients. As seen in IPD or PSP management, the staging of the disease process into early, middle, and late may provide a general framework for intervention to tackle the possible impairments, activity limitations, and participation restrictions of HD patients. However, the therapist should also understand that such staging is not watertight due to the progressive nature of the disease. In early-stage HD, patients may have issues such as poor endurance, limited physical activity, lack of motivation, anxiety and depression, apathy and sleep disturbance in the absence of obvious motor impairment, or specific limitations in functional activities. In the early stage, the therapy should aim at health education, advice for general promotion of strategies including education on safety, fatigue, and the timing of exercises, referral for exercise prescription, and evaluation of the baseline fitness level. With safety taken into account, gym or home-based aerobic exercises and strength training and task-specific functional activities can be encouraged. It is advisable to have a warm-up and a cool-down for the exercise program. Aerobic exercises may include walking, jogging, swimming, and biking, and strengthening exercises may include the use of progressive resisted strength training using weights or elastic bands or isokinetic devices. Frequency, duration, and intensity should be based on the baseline fitness level of the patient. Activities like balance training, core stability training, video-game and virtual reality-based exercises, and relaxation techniques can be recommended.

During the early toward the middle stage, impaired motor planning and programming may result in increased dependency on routine activities, difficulty in initiation and slowness in performing functional activities, including dressing and hygiene activities, and difficulty managing automatic tasks, such as sit-to-stand or walking. Therapy should aim to improve the ability to perform functional tasks and the speed of the tasks, maximizing safety. Visual, verbal, or other forms of cueing may help bypass the internal cueing mechanism to improve functional abilities. Cognitive movement strategies can also be advised during this phase to speed up the movements. When the mobility, balance, and risk of fall gradually become a concern due to hyperkinetic or hypokinetic movement abnormities, impaired balance reactions, reduced muscle strength, fatigue, and poor cognition, the physiotherapy should aim toward the maintenance of independent mobility, safe transfers, and reduction of fear of fall. Treatment should focus on strengthening exercises, general conditioning exercises, endurance training, balance training, and practicing transfers like sit-to-stand several times. Activities like throwing and catching a ball, self-initiated perturbations, and reach-out activities can be encouraged to improve the postural and balance reactions. The need for repeated practice of tasks in a specific environment, including gait training outdoors and obstacle training, may improve the functional mobility of the patient. Cues, including a metronome and lines on the

floor, may promote the rhythm, step initiation, step length, gait velocity, and gait symmetry. It is also advisable to train strategies on how to get up from the floor in case they fall. Periodical assessment is required to re-evaluate the balance and mobility of HD patient. At the appropriate time, the therapist should prescribe assistive devices and protective gear like helmets or elbow/knee pads to maximize safety during mobility.

In the middle stage, when secondary and adaptive changes and deconditioning develop, the patient's physical fitness level decreases, and participation in ADL reduces. Physical deconditioning is due to musculoskeletal and/or respiratory changes secondary to rigidity, dystonia, and chorea. Loss of ROM and loss of strength due to physical inactivity are certain musculoskeletal changes. During this stage, cognitive issues like memory deficits and lack of insight, psychological issues like anxiety and depression, and apathy may become additional challenges for rehabilitation. During this stage, promoting functional activities is the most effective way of maximizing the remaining ability. The frequency of falls also may increase due to the further progression of balance and gait dysfunctions. Stretching and flexibility exercises, encouraging patients to continue aerobic exercises and balance training, and teaching breathing exercises to maintain full respiratory function are certain treatment strategies that are advisable during this stage. Due to the involuntary movements, rigidity, and bradykinesia, the patient often tends to develop abnormal posturing even while sitting. Asymmetrical posturing may further reduce the joint ROM, flexibility and may induce further adaptive changes within the soft tissues. Improving postural control, specifically head control while sitting, is vital for communication, feeding, visual fixation, and balance activities. The treatment should also focus on preventing or limiting soft-tissue adaptation and skin breakdown. Positional stretching and use of custom-made chairs or wheelchairs with lateral support and straps can encourage a better alignment of the spine while sitting and also minimize the possibility of falls from the chair. In the later phase of the middle phase, active, assisted and passive range of motion exercises should be performed frequently to maintain the mobility of the joints. The use of splints is also recommended.

In the late stage, impaired respiratory function and capacity and poor airway clearance further restrict the functional abilities of the patient and predispose to chest infections. During this phase, optimizing the respiratory function for functional activities, improving the cardiorespiratory function, and augmenting secretion clearance are the general aims. Promoting functional exercise, positioning to manage breathlessness, promoting breathing exercises and use of airway clearance techniques, and encouraging relaxation techniques are some of the strategies to be adopted. In the latter part of the advanced stage, the patient will be completely dependent on all the functional skills with limited volitional control of limbs and trunk. The use of pressure-relieving mattresses and cushions for optimal positioning and regular and frequent change of position can reduce the possibilities of pressure sores and may provide a certain amount of comfort for the patient.

Further Reading

Allen NE, Canning CG, Sherrington C, Lord SR, Latt MD, Close JCT, et al. The effects of an exercise program on fall risk factors in people with Parkinson's disease: a randomized controlled trial. *Mov Disord*. 2010;25(9):1217-25.

Barone P, Santangelo G, Amboni M, Pellecchia MT, Vitale C. Pisa syndrome in Parkinson's disease and parkinsonism: clinical features, pathophysiology, and treatment. *Lancet Neurol.* 2016 Sep;15(10):1063-74.

Barry G, Galna B, Rochester L. The role of exergaming in Parkinson's disease rehabilitation: a systematic review of the evidence. *J Neuroeng Rehabil.* 2014;11:33.

Bello O, Sanchez JA, Lopez-Alonso V, Márquezet G, Morenilla L, Castro X, et al. The effects of treadmill or overground walking training program on gait in Parkinson's disease. *Gait Posture.* 2013;38(4):590-5.

Ben-Shlomo Y, Sieradzan K. Idiopathic Parkinson's disease: epidemiology, diagnosis and management. *Br J Gen Pract*. 1995;45:261-8.

Bunner KD, Rebec GV. Corticostriatal dysfunction in Huntington's disease: the basics. *Front Hum Neurosci.* 2016;10:317. Available from: https://doi.org/10.3389/fnhum.2016.00317.

Busse ME, Khalil H, Quinn L, Rosser AE. Physical therapy intervention for people with Huntington disease. *Phys Ther.* 2008;88:20-31.

Daroff RB, Jankovic J, Mazziotta JC, Pomeroy SL, editors. Bradley's Neurology in clinical practice. 7th ed. London: Elsevier; 2016.

Doherty KM, van de Warrenburg BP, Peralta MC, Silveira-Moriyama L, Azulay JP, Gershanik OS, et al. Postural deformities in Parkinson's disease. Lancet Neurol. 2011;10(6):538-549.

Donaghy M, editor. Brain's Diseases of the nervous system. 12th ed. New York: Oxford University Press; 2009.

Cano-de-la-Cuerda R, Pérez-de-Heredia M, Miangolarra-Page JC, Muñoz-Hellín E, Fernández-de-las-Peñas C. Is there muscular weakness in Parkinson's disease? *Am J Phys Med Rehabil.* 2010;89:70-6.

Clerici I, Ferrazzoli D, Maestri R, Bossio F, Zivi I, Canesi M, et al. Rehabilitation in progressive supranuclear palsy: effectiveness of two multidisciplinary treatments. *PLoS One*. 2017;12:e0170927.

Delwaide PJ. Parkinsonian rigidity. *Funct Neurol*. 2001;16:147-56.

Fok P, Farrell M, McMeeken J, Kuo YL. The effects of verbal instructions on gait in people with Parkinson's disease: a systematic review of randomized and non-randomized trials. *Clin Rehabil.* 2011;25:396-407.

Frenkel-Toledo S, Giladi N, Peretz C, Herman T, Gruendlinger L, Hausdorff JM. Treadmill walking as an external pacemaker to improve gait rhythm and stability in Parkinson's disease. *Mov Disord.* 2005;20(9):1109-14.

Fritz NE, Rao AK, Kegelmeyer D, Kloos A, Busse M, Hartel L, et al. Physical therapy and exercise interventions in Huntington's disease: A mixed methods systematic review. *J Huntingt Dis.*2017;6:217-35.

Galletly R, Brauer SG. Does the type of concurrent task affect preferred and cued gait in people with Parkinson's disease?. *Aust J Physiother.* 2005;51(3):175-80.

Gökçal E, Gür VE, Selvitop R, Yildiz GB, Asil T. Motor and non-motor symptoms in Parkinson's disease: effects on quality of life. *Arch Neuropsychiatry.* 2017;54(2):143.

Hass CJ, Buckley TA, Pitsikoulis C, Barthelemy EJ. Progressive resistance training improves gait initiation in individuals with Parkinson's disease. *Gait Posture.* 2012;35(4):669-73.

Huh YE, Kim K, Chung WH, Youn J, Kim S, Cho JW. Pisa syndrome in Parkinson's disease: pathogenic roles of verticality perception deficits. *Sci Rep.* 2018;8:1804. Available from: https://doi.org/10.1038/s41598-018-20129-2.

Keus SH, Munneke M, Nijkrake MJ, Kwakkel G, Bloem BR. Physical therapy in Parkinson's disease: evolution and future challenges. *Move Disord.* 2009;24:1-14.

Keus S, Munneke M, Graziano M, Paltamaa J, Pelosin E, Domingos J, et al. Physiotherapy guideline for Parkinson's disease. Netherlands: KNGF/ParkinsonNet (2014).
Kim HF, Hikosaka O. Parallel basal ganglia circuits for voluntary and automatic behaviour to reach rewards. *Brain.* 2015;138:1776-1800.
Lanciego JL, Luquin N, Obeso JA. Functional neuroanatomy of the basal ganglia. *Cold Spring Harb Perspect Med.* 2012;2:a009621. Available from: https://doi.org/10.1101/cshperspect.a009621.
Lee RG. Physiology of the basal ganglia: an overview. *Can J Neurol Sci.* 1984;11:124-8.
Lena F, Iezzi E, Etoom M, Santilli M, Centonze D, Foti C, et al. Effects of postural exercises in patients with Parkinson's disease and Pisa syndrome: a pilot study. *NeuroRehabilitation.* 2017;41:423-8.
Maiarú M, Garcete A, Drault ME, Mendelevich A, Módica M, Peralta F. Physical therapy in Wilson's disease: case report. *Phys Med Rehabil Int.* 2016;3(2):1082.
Marsden CD. Slowness of movement in Parkinson's disease. *Mov Disord.* 1989;4(1):S26-37.
McAuley JH, Daly PM, Curtis CR. A preliminary investigation of a novel design of visual cue glasses that aid gait in Parkinson's disease. *Clin Rehabil.* 2009;23(8):687-95.
Mirelman A, Herman T, Nicolai S, Zijlstra A, Zijlstra W, Becker C, et al. Audio-biofeedback training for posture and balance in patients with Parkinson's disease. J Neuroeng Rehabil. 2011;8:35.
Nieuwboer A, Rochester L, Muncks L, Swinnen SP. Motor learning in Parkinson's disease: limitations and potential for rehabilitation. *Parkinsonism Relat. Disord.* 2009;15:53-8.
O'Shea S, Morris ME, Iansek R. Dual task interference during gait in people with Parkinson disease: effects of motor versus cognitive secondary tasks. *Phys Ther.* 2002;82(9):888-97.
O'Sullivan S, Bezkor EW. Parkinson's disease. In: O'Sullivan SB, Schmitz TJ, Fulk GD, editors. 6th ed. Physical rehabilitation. Philadelphia: FA Davis Co; 2014. p.807-58.
Petzinger GM, Fisher BE, Van Leeuwen JE, Vukovic M, Akopian G, Meshul CK, et al. Enhancing neuroplasticity in the basal ganglia: the role of exercise in Parkinson's disease. *Mov Disord.* 2010;25(Suppl 1):141-5.
Pohl M, Rockstroh G, Rückriem S, Mrass G, Mehrholz J. Immediate effects of speed-dependent treadmill training on gait parameters in early Parkinson's disease. *Arch Phys Med Rehabil.* 2003;84(12):1760-6.
Poujois A, Mikol J, Woimant F. Wilson disease: brain pathology. *Handb Clin Neurol.* 2017;142:77-89.
Quinn L, Kegelmeyer D, Kloos A, Rao AK, Busse M, Fritz NE. Clinical recommendations to guide physical therapy practice for Huntington disease. *Neurology.* 2020;94:217-28.
Rochester L, Burn DJ, Woods G, Godwin J, Nieuwboer A. Does auditory rhythmical cueing improve gait in people with Parkinson's disease and cognitive impairment? A feasibility study. *Mov Disord.* 2009;24(6):839-45.
Ropper AH, Samuels MA, Klein JP, Prasad S, editors. Adams and Victor's Principles of neurology. 10th ed. New York: McGraw Hill Education; 2014.
Schenkman M, Butler RB. A model for multisystem evaluation treatment of individuals with Parkinson's disease. *Phys Ther.*1989;69:932-43.
Slade SC, Finkelstein D, McGinley J, Morris ME. Exercise and physical activity for people with progressive supranuclear palsy: A systematic review. *Clinical Rehabil.* 2020;34(1):23-33.
Steiner H, Tseng K-Y. Handbook of basal ganglia structure and function. London: Academic; 2010.
Strouwen C, Molenaar EA, Münks L, Keus SHJ, Bloem BR, Rochester L, et al. Dual tasking in Parkinson's disease: should we train hazardous behavior? *Expert Rev Neurother.* 2015;15:1031-9.
Takakusaki K, Saitoh K, Harada H, and Kashiwayanagi M. Role of basal ganglia-brainstem pathways in the control of motor behaviors. *Neurosci Res.* 2004;50:137-51.
Turnbull GI, editor. Physical therapy management of Parkinson's disease. New York: Churchill Livingston;1992.

Turnbull GI, Millar J. A proactive physical management model of Parkinson's disease. *Top Geriatr Rehabil.* 2006;22(2):162-71.

van der Kolk NM, King LA. Effects of exercise on mobility in people with Parkinson's disease. *Mov Disord.* 2013;28(11):1587-96.

Vojciechowski AS, Zotz TGG, Loureiro APC, Israel VL. The international classification of functioning, disability and health as applied to Parkinson's disease: a literature review. *Advances in Parkinson's Disease.* 2016;5:29-40. Available from: https://doi.org/10.4236/apd.2016.52005.

Walshe JM. History of Wilson's disease: 1912 to 2000. *Mov Disord.* 2006;21:142-7.

Willems AM, Nieuwboer A, Chavret F, Desloovere K, Dom R, Rochester L, et al. The use of rhythmic auditory cues to influence gait in patients with Parkinson's disease, the differential effect for freezers and non-freezers, an explorative study. *Disabil Rehabil.* 2006;28(11):721-728.

Yen CY, Lin KH, Hu MH, Wu RM, Lu TW, Lin CH. Effects of virtual reality-augmented balance training on sensory organization and attentional demand for postural control in people with Parkinson disease: a randomized controlled trial. *Phys Ther.* 2011;91(6):862-74.

Zampieri C, Di Fabio RP. Balance and eye movement training to improve gait in people with progressive supranuclear palsy: a quasi-randomized clinical trial. *Phys Ther.* 2008;88:1460-73.