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Chapter 7

Gait, postural instability, and freezing

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INTRODUCTION

A chapter on gait and balance impairment is inevitable in this book on non-motor and non-dopaminergic features of Parkinson’s disease (PD), for several reasons. First, even though gait impairment and postural instability (jointly referred to in this chapter as “axial motor disability”) are traditionally regarded as “motor” features of PD, evidence is accumulating that our ability to walk or maintain balance are, at least in part, also governed by cognitive processes. For example, many PD patients find it difficult to walk and talk at the same time, and when they nevertheless try to combine these two seemingly easily tasks, a fall is often the result. Also, the appearance of axial motor disability typically coincides with cognitive decline, as becomes obvious in patients with the so-called PIGD (postural instability and gait disability) subtype of PD. This co-occurrence could be a chance finding, simply reflecting the more widespread disease pathology in this subtype of PD. But an interesting alternative explanation is that patients may only begin to fall when they fail to consciously compensate for their axial motor deficits. In its most striking form, this is seen in patients with progressive supranuclear palsy (PSP) who have an unusually high risk of falling, not only because their balance is so poor, but also because they fail to adjust their behaviour due to lack of insight – a feature sometimes referred to as “motor recklessness”. Taken together, these observations suggest that difficulties with gait or balance are perhaps more “non-motor” than one might have initially thought.

Second, axial disability can rightly be included among the non-dopaminergic features of PD. Gait impairment and postural instability are typically “late” features of PD, appearing at a time when the disease extends well beyond the dopaminergic substantia nigra. Several observations support a non-dopaminergic basis for axial motor disability in PD. Axial motor features are typically inadequately controlled with dopaminergic medication. This is particularly the case for postural instability and, to a lesser extent, also for gait abnormalities. Indeed, most falls in PD occur when patients are in their ON state. Such clinical observations have been tested with dynamic posturography: evaluating balance quantitatively while upright standing subjects are perturbed by sudden movements of a support surface. The results suggest that several balance problems (mainly the reactive automatic postural responses) in PD are not primarily dopamine-dependent. In fact, dopaminergic medication can paradoxically increase the frequency of falls by inducing ON period freezing, or orthostatic hypotension leading to syncopal falls, or violent dyskinesias that can literally throw the patients off their feet.

Third, neuropathological and biochemical studies suggest that non-dopaminergic lesions emerge at about the same time when gait and balance problems develop. Specifically, post-mortem brain studies in patients with gait and balance impairment demonstrate substantial cell loss within the locus coeruleus, particularly the caudal part.
that projects mainly to the spinal cord and cerebellum.\textsuperscript{21,22} Consistent with this cell loss in the locus coeruleus, CSF analyses and post-mortem brain studies have shown reduced norepinephrine levels in PD. Further, there is a relation between the reduced concentration of norepinephrine and the severity of gait and postural disturbances, and levels of norepinephrine are significantly reduced in PD patients with freezing of gait.\textsuperscript{23} Gait impairment, especially freezing (and possibly also balance abnormalities) may further be linked to dysfunction of the mixed cholinergic-glutamatergic pedunculopontine nucleus (PPN) in the dorsal brainstem.\textsuperscript{24,25,26} The PPN normally governs step initiation and step maintenance. PPN dysfunction is caused partially by excessive inhibition from the internal globus pallidus and substantia nigra pars reticulata. In addition, cell loss occurs within the cholinergic portion of the PPN, and this neurodegeneration likely further aggravates the gait problems.\textsuperscript{26}

Observations in patients with atypical parkinsonism provide a final argument to support a non-dopaminergic basis for axial motor disability in PD. Generally, gait and balance problems emerge earlier and are more prominent in patients with atypical parkinsonism; this includes patients with progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD), dementia with Lewy bodies (DLB) and vascular parkinsonism.\textsuperscript{5,27,28} These atypical parkinsonian syndromes are all typically characterised by more widespread pathology compared to PD, including abundant extranigral and non-dopaminergic lesions.

This is not to say, of course, that gait and balance problems can be ascribed entirely to the presence of non-dopaminergic lesions. For many patients, dopamine replacement therapy can provide a partial benefit, particularly in early stages of the disease, and more so for gait than posture or balance. The bradykinetic gait in early disease stages – characterized by a reduced walking velocity and small, shuffling steps – usually improves with dopaminergic treatment. And freezing of gait – which usually appears later in the course of the disease – will also improve in most patients when dopaminergic therapy is started or augmented.\textsuperscript{17,29} Freezing may become more resistant in later stages of the disease, but the issue here may be related to inadequate dosing: because of adverse effects of treatment such as response fluctuations or hallucinations. Indeed, it has been our clinical impression that the threshold to obtain a therapeutic response may be higher for freezing compared to other motor signs (Figure 1) This could partially explain the presence of ON period freezing of gait: at certain doses most motor signs will have improved, but freezing persists, falsely creating the impression that medication actually induced the freezing symptoms. A link to dopaminergic lesions was recently made in a large prospective aging study, were during post-mortem examination of brains of 50 subjects without PD detected an association between cell loss in the dorsolateral quadrant of the substantia nigra and UPDRS scores for postural instability, stooped posture and gait disturbances.\textsuperscript{30}
The most devastating consequence of gait and balance impairment is falling. In this chapter, we summarize the dominant clinical features of axial motor disability in PD, provide a pathophysiological framework for falls in PD, and consider how to develop an individually tailored and multifactorial falls prevention program. We propose a battery of measures that are based on published observations in PD, personal experience and knowledge obtained with falls prevention in the elderly. The protocol proposed here may serve both as a guide for current clinical use, and also as a basis for future formal evaluation in adequately designed randomised clinical trials.

**CLINICAL ASSESSMENT OF BALANCE AND GAIT**

**Importance**

Careful recognition of gait and balance abnormalities is crucial, for several reasons (Table 1). First, axial features can often assist clinicians in refining their differential diagnosis in patients presenting with a hypokinetic-rigid syndrome. It is not rare for the specific gait or balance features to provide the clue to the diagnosis. Examples include the occurrence of

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**Fig 1** Treatment of freezing of gait, in relation to other motor symptoms and signs. The threshold for symptoms and signs to improve may be lower for appendicular manifestations of PD (a), compared with the threshold for freezing of gait to improve (b). This creates an intermediate level, occurring at doses where patients generally appear to respond well to medication, but nevertheless experience freezing of gait. Although counterintuitive, we recommend first increasing the dose of anti-parkinson medication in these patients, provided that they do not experience dose-limiting side effects. If freezing improves, the patient actually has “pseudo ON” freezing. If freezing worsens, the patient has true ON period freezing, and the dose should be reduced.
of seemingly spontaneous backward falls in the first year of the disease – suggesting a diagnosis of PSP – or the presence of dominant lower-body parkinsonism with early and levodopa-resistant freezing of gait – suggesting a diagnosis of vascular parkinsonism. Second, as indicated earlier, careful clinical assessment provides the basis for subsequent treatment, aimed at improving gait and balance, reducing or preventing falls, and minimizing their consequences. Indeed, falls in PD often have devastating consequences, leading to a poor overall prognosis. Hip fractures appear in about 25% of patients within 10 years after the diagnosis and are associated with high morbidity, admission to nursing home, and mortality. Fractures of the wrist seem less common, perhaps because the hands are not stretched out fast enough after a fall. “Minor” injuries such as bruises

<table>
<thead>
<tr>
<th>Table 1 Importance of gait and balance assessment in clinical practice</th>
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<tr>
<td><strong>Importance of gait and balance assessment in clinical practice</strong></td>
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<tr>
<td>Support for the differential diagnosis</td>
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<td>Basis for individually tailored treatment</td>
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<td>Prevention of complications</td>
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<td>– Falls</td>
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<td>– Constipation</td>
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<td>– Pressure sores</td>
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<td>– Insomnia</td>
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<td>– Osteoporosis</td>
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<td>– Physical inactivity</td>
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<td>– Loss of independence</td>
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<td>– Social isolation</td>
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<td>– Fear of falling</td>
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<td>– Reduced quality-of-life</td>
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<td>– Caregiver stress</td>
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<td>Marker of poor prognosis/greater disease severity and associated symptoms</td>
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<td>– Depression</td>
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<td>– Anxiety</td>
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<td>– Rapid disease progression</td>
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<td>– Urinary incontinence</td>
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<td>– Cognitive decline</td>
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<td>– Nursing home admission</td>
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<td>– Reduced survival</td>
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<tr>
<td>Marker for underlying abnormalities</td>
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<tr>
<td>– Frontal executive deficits</td>
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<tr>
<td>– Underlying cerebrovascular disease</td>
</tr>
<tr>
<td>Socio-economic impact</td>
</tr>
<tr>
<td>– Loss of productivity</td>
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<td>– Costs related to injuries</td>
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or lacerations are even more common than fractures. Furthermore, reduced mobility is associated with other incapacitating complications, including constipation, pressure sores, insomnia and osteoporosis, which in turn increases the fracture risk. Immobility also deprives patients of their independence and social contacts. These problems are aggravated by a commonly present and incapacitating fear of renewed falls. When this fear of falling becomes excessive, patients become unnecessarily immobilized, with great consequences for their social interactions as well as their physical fitness.

Third, the presence of gait and balance abnormalities can serve as a marker for other signs that are perhaps less obvious during routine clinical examination, such as frontal executive deficits or underlying cerebrovascular disease. This will be discussed in more detail in the section on clinical manifestations.

Fourth, gait and balance abnormalities have considerable prognostic importance. In a large group of 362 patients who were originally enrolled as part of the DATATOP study and who were carefully followed for disease progression, the level of gait dysfunction did not predict future changes in health-related quality of life. However, worsening gait and balance over time were accompanied by worsening mental as well as physical health-related quality of life, underscoring the need to preserve balance in order to prevent a worsening of health-related quality of life. Furthermore, a prior fall remains the best predictor of future falls, and postural instability and falls are associated with a reduced survival. This increased mortality is explained by the occurrence of lethal falls and by secondary immobilization, which reduces general fitness and increases the risk of cardiovascular disease. Importantly, the disease also progresses at a faster rate once falls are present.

And finally, gait and balance abnormalities have implications for society at large. Falls and fall-related injuries are extremely costly and contribute to the overall costs of PD. Falls are also a major reason for caregiver stress, and health care costs rise considerably when the caregiver support collapses.

In the light of these considerations, it should be appreciated that the clinical examination of parkinsonian patients is incomplete without a proper gait and balance assessment. Whenever possible, patients should be examined during both the OFF state (preferably following withdrawal of antiparkinson medication for at least 12 hours) and the subjective “best ON” state. It is recommended to have a sufficiently large examination room, or else to take the patients to the corridor to examine their gait. At the same time, gait and balance need to be challenged using a series of specific tests, in order to bring about the full range of abnormalities. Note that performance is usually much better in the hospital, where lighting is optimal and gait is rarely complicated by obstacles in the pathway. Hospital examination is also obscured by a phenomenon termed “kinesia paradoxica”, namely the ability of poorly mobile patients with advanced disease to move unexpectedly well under emotional circumstances sometimes (which a doctor’s visit). In contrast, at home patients are more at ease, and they need to walk in crowded living rooms (forc-
ing them to make narrow turns), with poor lighting or loose rugs on the floor. Some of these domestic factors can be copied in the examination room, for example by forcing patients to turn around in tight quarters to provoke freezing. Nevertheless it is often very informative when a physiotherapist or occupational therapist pays a home visit and to witness the patients’ performance in their own habitat.

Gait
For most patients, walking already changes can already be detected in early stages of the disease, and can even be the presenting symptom, for example an asymmetrically reduced or absent arm swing. Other early features include difficulties turning around in a standing or recumbent position. As the disease progresses, gait becomes slower and the typical parkinsonian gait emerges with shuffling and short steps, a bilaterally reduced arm swing and slow turns which are executed en bloc. In contrast to most other gait disorders, gait is typically not wide-based. Presence of a broad-based gait generally suggests presence of atypical parkinsonism. A simple test is asking patients to take 10 consecutive tandem steps; patients with idiopathic PD can usually perform this without difficulty, even when moderately severely affected. Hence, taking even a single corrective side step is suggestive for atypical parkinsonism, particularly in early stages of the disease. Note that patients may compensate for their “automatic” gait problems by paying conscious attention to the act of walking. Distraction or asking the patient to perform a double or secondary task (answering questions, carrying an object) interferes with this compensatory strategy and often aggravates the gait disorder, causing patients to slow down or completely stop walking.

Freezing of gait
The features described above represent a form of “continuous” gait abnormality: they are more or less consistently present. In addition, PD patients can also experience “episodic” gait disorders, that is, walking problems that are only irregularly present, intermingled with periods when gait is much better. The prime example of these episodic gait disorders is freezing of gait, when patients experience sudden and usually brief moments where the feet subjectively become “glued to the floor”. For practical purposes, freezing of gait was recently defined as “a brief episode during which patients find it impossible to generate effective forward stepping movements, in the absence of another cause than parkinsonism or higher cortical deficits”. The prevalence of freezing increases with disease duration and progression of disease severity, although it can be present in early stages of PD, and occasionally even at disease onset. However, early freezing episodes should generally alert the clinician to the presence of a form of atypical parkinsonism, or a disorder called primary progressive freezing of gait. In patients with PD, freezing is more common after prolonged dopaminergic treatment, but this does not necessarily implicate that the drugs are causally related to freezing (because more severe symptoms...
Gait, postural instability, and freezing also require more medication). Indeed, freezing can occur in drug-naive patients, and most forms of freezing in PD improve with dopaminergic medication. Note that freezing is also common in other parkinsonian disorders (e.g. PSP, MSA, vascular parkinsonism and normal pressure hydrocephalus). However, freezing is rare in drug-induced parkinsonism.

Freezing most commonly appears while patients are making turns, in particular narrow turns in tight quarters. Other circumstances that commonly provoke freezing include negotiating a narrow passage such as a door, trying to initiate gait (“start hesitation”), executing a double task (such as talking while walking) or upon reaching a target. It is less common for freezing to occur during straight, undisturbed walking. Although the name perhaps suggest otherwise, freezing is usually not a complete “immobile” blockade of walking movements (complete akinesia), but is a much more dynamic phenomenon. The most common presentation is with shuffling small steps, or a characteristic “trembling” of the legs, with the frozen foot in plantar flexion and the forefoot stuck to the floor. Freezing of just one leg may occur, particularly while turning. Most freezing episodes are brief, usually lasting only several seconds or less, although in more advanced stages of the disease freezing may persist for minutes. Freezing episodes are also much briefer during the ON phase, compared to the OFF phase.

Detection of freezing often depends on a careful history taking, with detailed enquiry about the feeling of being glued, and attention to the provoking circumstances. It can be difficult to assess freezing reliably during physical examination, because the anxiety associated with the doctor’s visit may suppress the phenomenon. A freezing of gait questionnaire has been developed for this purpose. There is now an updated version where patients and their immediate carers are shown video clips of characteristic freezing events, in order to facilitate recognition of the phenomenon. This updated questionnaire also addresses the impact of freezing on daily life, for example fear of falling.

Physical examination should include a dedicated “freezing of gait trajectory” that features specific triggers to elicit freezing: gait initiation; undisturbed walking in an open space; and walking under challenging situations (crossing a door or other narrow space, turning around, negotiating obstacles and performing a dual task) (Figure 2). Interestingly, many patients only experience freezing during full turns (360 to 540°) and not during partial turns (180°), so a standardized gait trajectory should include full turns (in both directions, because freezing often shows a directional sensitivity, being much worse and sometimes even exclusively present for turns in one direction). In addition to such attempts to provoke freezing, it is also useful to evaluate the response to external cues. This may have diagnostic importance, because freezing will improve in PD patients, but generally not in patients with higher-level gait disorders. Evaluating the effect of cues may also help to determine possible therapeutic interventions. Finally, various quantitative gait assessments have been proposed, but these methods do not yet have a proven value for clinical practice.
Changes in posture can provide important diagnostic information. A gently stooped posture can be seen in early stages of PD, and this becomes more pronounced in later stages of the disease, usually with some lateral leaning of the trunk. However, severe and persistent lateroflexion – the so-called “Pisa syndrome” or pleurothotonus – often (but not always) suggests neuroleptic-induced dystonia, MSA or post-encephalitic parkinsonism. Camptocormia refers to a marked anteflexion of the thoracolumbar spine between 30 to 90 degrees, but without forward flexion of the neck. This can occur in both PD (where it may occasionally improve with dopaminergic medication or deep brain surgery) and forms of atypical parkinsonism. Camptocormia is apparent on standing, worsens while walking, but decreases while sitting and even disappears when patients are lying down. This latter feature separates camptocormia from the fixed kyphoscoliosis seen in patients with degenerative changes of the spine. An extreme degree of antecollis relative to other body parts, with the neck held in a relatively fixed and severely flexed position, or when the chin touches the chest, is unusual and suggests a diagnosis of MSA. Antecollis develops in about half of pathologically proven MSA patients, usually in the middle or late stages of the disease. In contrast, retroflexion of the neck (retrocollis) suggests a diagnosis of PSP, but this is usually not an early feature. In PSP axial rigidity of the neck is higher than in the trunk, whereas the opposite pattern occurs in PD.
Postural stability is preserved early in the course of PD, and falls never occur at onset or within the first two years of the disease in pathologically confirmed cases of idiopathic PD.\textsuperscript{28} Balance impairment gradually develops as the disease progresses\textsuperscript{68}, appearing later (and in less prominent form) in patients with the tremor-dominant type of PD. Being unable to stand on one leg, for example while getting dressed, is often one of the earliest signs of postural instability.

A battery of clinical tests is needed to capture the complex nature of balance problems in patients with basal ganglia disorders. Functional “everyday” tests should be performed whenever possible. These include rising from a chair, sitting down and getting in and out of a bed. It is particularly important to test the so-called defensive balance reactions, which are evoked by imminent falls. Examples include the ability to take corrective steps or to make protective arm movements (to grasp for support, or to cushion the impact of an impending fall). Evaluation of these defensive reactions is often difficult in a clinical setting because patients must be brought close to (or even beyond) their limits of stability. Quantified assessment following standardized balance perturbations – using dynamic posturography – is perhaps more suited for this purpose, although the clinical utility for the management of individual patients remains unclear.\textsuperscript{69} In clinical practice, the retropulsion test is typically used to test defensive reactions, but this test is not without problems. There is great variability in test performance across clinicians (depending on subjective preferences, but also on height or weight of both the patient and investigator), scoring of the response is subjective, and its interpretation is not straightforward. For example, it is unclear how many corrective steps can still be regarded as “normal”. Interestingly, taking more steps is usually equated with greater balance impairment, but this may not be correct because corrective steps are important defensive reactions. Indeed, the most abnormal reaction is not taking any corrective step at all, leading to a fall “like a pushed toy soldier” (note that freezing can be a “confounder” here, interfering with the ability to step backward and leading to a fall “like a log” into the arms of the investigator, even when balance itself is otherwise preserved). We recommend taking the speed and quality of balance reactions into account (rather than merely counting the number of corrective steps), and to regard a slow response as abnormal even if only one or two steps are taken. A particular problem is the inconsistency in the strength of the shoulder pull, within and between raters (depending on experience or physical strength), as well as within and between patients who may have different degrees of instability. Consequently, the retropulsion test has an only moderate intra- and inter-rater consistency, correlates poorly to objective measures of postural instability (as quantitatively ascertained in a balance laboratory) and is a poor predictor of actual falls in daily life.\textsuperscript{70} We usually deliver one shoulder pull without specific prior warning, as this may best mimic daily life circumstances where falls are usually unexpected events. We then repeat the test several times and regard failure to “habituate” to the test as another sign of bal-
ance impairment. As such, the retropulsion test indexes the degree of postural instability. However, the test fails to predict falls, at least in PD, probably because falling is the net result of a complex interplay between gait, balance and protective mechanisms. The “Push and Release” test was recently proposed as a more consistent and apparently also more sensitive alternative to the pull test (or retropulsion test). The essence is to eliminate the inconsistency of the stimulus by instructing subjects to actively push backward against the palms of the examiner’s hands (placed on the subject’s scapulae), allowing the trunk to move backward while the examiner supports the subject’s weight. Balance is then perturbed when the examiner suddenly removes the external support, forcing the patient to take a backward step to regain balance. The first experience showed that the “Push and Release” test correlated better with self-reported prior falls, when compared with the retropulsion test, and that it could be used in both the ON and the OFF states. A drawback of this Push and Release test is that patients may have difficulties following the instructions, and some are hesitant to adequately push back into the examiner’s hands due to lack of confidence.

Falls
Falls are a devastating consequence of postural and gait disturbances. Prospective surveys in PD note high rates of falls that exceed those of community-dwelling elderly subjects. The incidence of falls is even higher when near-falls are included, and these near-falls typically precede the onset of actual falling. The risk of falling is highest when patients reach Hoehn and Yahr stage 2.5 to 3, when balance becomes impaired but patients are still sufficiently mobile to be at risk of falling. In these moderately affected PD patients, the risk of sustaining a single fall was six times higher than in healthy age-matched peers, and the risk of sustaining recurrent falls was nine times higher. The falling rate may level off in later stages of the disease due to disease progression and increasing immobility. Indeed, patients in Hoehn and Yahr stage 5 are bound to their bed or wheelchair are for this reason unlikely to fall. Furthermore, patients may compensate for their worsening balance by moving slower and purposely restricting their activities.

It is important to realize that most falls occur when patients are in their ON state, possibly reflecting their increased mobility. This observation also underscores that dopaminergic medication usually provides little or no improvement of postural instability. In fact, dopaminergic medication can cause dyskinesias that may perturb patients and increase falls. In addition, medication may cause or aggravate cognitive dysfunction, for example by causing delirium and risky wandering behaviour, leading to more falls. Most falls involve movements of the trunk, in particular sudden turning movements, presumably because this provokes freezing. Changes in posture (“transfers”), such as rising from a chair, are also commonly responsible. Orthostatic hypotension has been mentioned as an independent risk factor for falls in PD. However, falls due to preceding loss of consciousness
are rare, and when this occurs clinicians should consider MSA, where syncope due to autonomic dysfunction is common.⁷⁶

**Cognitive deficits**

PD patients with gait and balance problems should always receive a cognitive examination, especially testing the frontal executive functions and attention. This may seem unnecessary, because gait and balance control are traditionally considered to be a largely automatic process, governed mainly at a subconscious level by spinal and perhaps some brain stem neural structures. However, recent studies have shown that neuropsychological processes such as attention are necessary for adequate balance maintenance. Walking is an even more complex process than standing, involving a range of cognitive systems.⁷⁷

This role of cognition is obvious during many activities of daily living, when people need to perform multiple actions simultaneously or quickly shift attention and control from one task to another. To perform such actions, cognitive abilities are needed to effectively monitor the environment, choose flexible response patterns to appearing threats and to make appropriate motor responses necessary for completing goals - and this is precisely where patients with PD experience great difficulties, perhaps explaining why gait and balance deficits are such prominent features of PD. Indeed, cognitive dysfunction is particularly prominent in patients with the PIGD subtype of PD.²³⁷⁸ And it may also explain why falls seem to be particularly prominent in disorders that are characterized by a combination of both motor deficits (gait impairment, postural instability) plus a concurrent decline in cognitive functions. PD itself is one good example, but there are many other such disorders, including various forms of atypical parkinsonism (PSP, Lewy body dementia, vascular parkinsonism), and Alzheimer’s disease.⁷⁹

Patients with PD have difficulty executing two different motor tasks simultaneously, such as walking and carrying an object, and these dual task problems are associated with the risk of falling.¹ Various studies have shown that frontal executive dysfunction is related to gait impairment in PD patients and is associated with an increased risk of falls.⁹⁰ Moreover, frontal executive dysfunction and freezing frequently co-occur, but there is as yet no proof of a direct causal interrelationship.³⁶ Recklessness, decreased ability to learn cues and an increased sensitivity to cognitive overload (for example when dual tasking) may explain why patients with frontal executive dysfunction are more prone to falls. Moreover, the presence of frontal executive dysfunction may give a clue to the underlying aetiology, as it is more prominent in atypical parkinsonism than in idiopathic PD. A clear example is provided by patients with PSP, where “motor recklessness” combined with progressive balance deficits are jointly responsible for the high rates of falls.⁵ Finally, other mental functions should also be examined. Depression is associated with falls, and possibly increased freezing, and freezing is also associated with anxiety and panic attacks.⁹²
TREATMENT

A multifactorial falls prevention program

Adequate treatment of gait and balance impairment is crucial in view of their potentially devastating consequences. The key goals should be prevention, preservation of a safe mobility and independence. We have recently reviewed the specific medical and non-medical treatment options of specific gait and balance problems in PD. Rather than reiterating these treatment recommendations, we focus on a newly developed protocol for a multidisciplinary falls prevention program. To achieve this, it is particularly important to consider the pathophysiology of falls, as this offers a rationale for preventive strategies. Falls in PD patients are usually not just caused by a single factor – such as a reduced step height – but are typically the net result of a complex and multifactorial pathophysiology. This pathophysiology includes both “extrinsic” or environmental factors (e.g. loose rugs on the floor) and “intrinsic” or patient-related factors (including balance impairment and gait disability, in particular freezing of gait). Many of these factors are specific for PD, but patients may also fall due to generic risk factors for falls that apply to any elderly person (‘generic risk factors’).

It is therefore unlikely that, just by themselves, single interventions will be able to prevent patients from falling. Instead, we anticipate that a multifactorial falls prevention program will be needed, including PD-specific therapeutic measures plus a set of generic strategies. The merits of such a comprehensive falls prevention program have never been evaluated in PD, and in fact, there is no accepted menu of the most effective interventions. Here we will propose such a program, based on (a) determination of previously identified risk factors for falls in PD and (b) determination of those factors that are potentially amenable to therapeutic intervention. We subsequently tailored a menu of therapeutic interventions to address risk factors, including not only disease-specific strategies, but also a selection of “generic” falls prevention strategies derived from the literature and from published national and international falls prevention guidelines (Table 2). A challenge here was to identify therapeutic strategies that would be both relevant and feasible for PD patients. For example, standing with both legs crossed is an accepted intervention to reduce falls caused by orthostatic hypotension, but is unlikely to be an acceptable treatment for PD patients given their postural instability. Also, each falls prevention strategy needs to strike a balance between being both comprehensive (covering every single potential risk factor) and tolerable (in being not too demanding for PD patients, given their fatigue and at times limited learning abilities). Based on these considerations, we have constructed a concept for a Multifactorial Parkinson Falls Prevention Strategy that accommodates all of the above factors. This protocol is summarized in Table 2. We will briefly discuss a few elements of the multifactorial strategy.
Table 2 Selected generic and disease-specific risk factors for falls, and tailored interventions.

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<thead>
<tr>
<th>Risk factor for falls</th>
<th>Tailored intervention</th>
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<tr>
<td><strong>PD-specific</strong></td>
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<tr>
<td>Gait impairment (e.g. reduced step height)</td>
<td>· Increase antiparkinson medication</td>
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<tr>
<td></td>
<td>· Physiotherapy (cueing strategies) (94;95)</td>
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<tr>
<td>Freezing of gait</td>
<td>· Optimize antiparkinson medication</td>
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<tr>
<td></td>
<td>· ON phase freezing: decrease levodopa</td>
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<td></td>
<td>· OFF increase freezing: increase levodopa; MAO-blocker</td>
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<tr>
<td></td>
<td>· Physiotherapy (cueing strategies) (94;95)</td>
</tr>
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<td></td>
<td>· Eliminate domestic hazards (96)</td>
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<tr>
<td>Postural instability</td>
<td>· Optimize antiparkinson medication (usually ineffective)</td>
</tr>
<tr>
<td></td>
<td>· Physiotherapy (balance training) (94)</td>
</tr>
<tr>
<td></td>
<td>· Lower limb strength training (97)</td>
</tr>
<tr>
<td>Bradykinesia (e.g. slow protective arm movements)</td>
<td>· Increase dopaminergic medication</td>
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<tr>
<td>Dyskinesias</td>
<td>· Optimize antiparkinson medication</td>
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<td>Inability to handle dual tasks</td>
<td>· Avoiding dual tasks (physiotherapy, occupational therapy) (1;89)</td>
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<td></td>
<td>· Cognitive movement strategies (chaining) (94)</td>
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<td>Transfers</td>
<td>· Increase antiparkinson medication</td>
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<td></td>
<td>· Cognitive movement strategies (94)</td>
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<td><strong>Generic</strong></td>
<td></td>
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<tr>
<td>Polypharmacy</td>
<td>· Reduction of medication (consult a geriatrician)</td>
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<tr>
<td>Sedative drugs (benzodiazepines)</td>
<td>· Stop when possible</td>
</tr>
<tr>
<td>Daily use of alcohol</td>
<td>· Minimize alcohol intake</td>
</tr>
<tr>
<td>Fear of falling</td>
<td>· Increase balance confidence (94)</td>
</tr>
<tr>
<td>Impaired ADL</td>
<td>· Occupational therapist (96)</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>· Physiotherapy: improve physical capacity, muscle power, mobility, muscle length (94)</td>
</tr>
<tr>
<td>Improper use of assistive device</td>
<td>· Train use of assistive devices (physical therapist; occupational therapist)</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>· Consult eye specialist</td>
</tr>
<tr>
<td></td>
<td>· Restrict use of multifocal glasses</td>
</tr>
<tr>
<td></td>
<td>· Cataract surgery (98)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>· Medication (no evidence for PD to reduce falls)</td>
</tr>
<tr>
<td></td>
<td>· Cholinesterase inhibitor</td>
</tr>
<tr>
<td></td>
<td>· Physiotherapy</td>
</tr>
<tr>
<td></td>
<td>· Avoid multitasking</td>
</tr>
<tr>
<td></td>
<td>· Minimize hazardous behaviour</td>
</tr>
<tr>
<td>Behavioural disturbances</td>
<td>· Atypical neuroleptics</td>
</tr>
<tr>
<td></td>
<td>· Restriction of activities (only if all other measures fail)</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>· Muscle strength training (94;97;99)</td>
</tr>
</tbody>
</table>
Medication

As outlined at the outset of this chapter, dopaminergic medication has mixed effects on gait, balance and falls. On the one hand, some axial motor features can improve following treatment with dopaminergic medication. For example, freezing is usually seen during the OFF state, and such OFF state freezing of gait may improve when dopaminergic medication is increased. However, other gait and balance problems are more resistant to treatment or are even aggravated by dopaminergic medication. It is therefore important to review carefully the relation between falls and the timing of intake of dopaminergic medication. When freezing appears to occur during the ON state – which is the case in only a small proportion of PD patients – the first step is to nevertheless further increase the dose of dopaminergic therapy, as some patients actually have “pseudo-ON freezing” (see Figure 1). In a few patients, freezing will worsen further, suggesting it is a true ON period sign, and this necessitates a dose reduction. Benzodiazepines and other sedative medication also need to be avoided whenever possible, as this may further increase the risk of falling.

Pharmacotherapy of gait and balance problems should ideally aim at correction of both dopaminergic and non-dopaminergic deficits. Attention is now shifting towards development of ‘non-dopaminergic’ drugs directed at other neurotransmitter systems. Unfortunately, such drugs are not yet available for treatment of axial disability.

Physiotherapy

There is increasing evidence to support the use of physiotherapy as part of a comprehensive falls prevention program. Patients who have difficulties with initiating or maintaining gait often report that simple tricks can promote walking; these include clues that are environmental (e.g. stepping over an object on the floor) or generated (e.g. counting). This technique of using internal or external cueing can be exploited by physiotherapists, who can train patients to use auditory cues (such as listening to rhythmic

<table>
<thead>
<tr>
<th>Risk factor for falls</th>
<th>Tailored intervention</th>
</tr>
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</table>
| Postural hypotension | · Decrease antiparkinson medication  
· Decrease other hypotensive medication (100)  
· Increase dietary salt and fluid intake  
· Anti-orthostatic manoeuvres (if balance is good)  
· Pressure stockings  
· Small meals  
· Raising cranial end of the bed  
· Symptomatic medication:  
· Fludrocortisone  
· Midodrine |

| Urinary incontinence and nocturia | · Reduce coffee and alcohol in the evening  
· Adequate night-time lighting  
· Incontinence materials |

| Environmental risk factors | · Occupational therapy at home |

Table 2 Selected generic and disease-specific risk factors for falls, and tailored interventions. (continued)
sounds of a metronome), visual cues (such as stepping over lines pasted onto the floor), tactile cues (such as tapping on the leg) or mental cues (such as simple arithmetic, or generating a mental image of the appropriate step length). Physiotherapists can also teach patients how to handle their freezing episodes. The risk of falling appears highest in patients who actively try to “overcome” their gait blockade, so patients should be instructed to simply wait for the freezing to disappear. Physiotherapists can also address the cognitive aspects of falling, for example by teaching patients to avoid multitasking in daily life, and to split complex tasks into several less complex sub-movements (a technique called “chaining”). Such cognitive movement strategies have been shown to improve transfers or rolling over in bed in PD patients. Another approach is to restore balance confidence and diminish the fear of falling. This may help to restore mobility and promote independence. There is no specific evidence for PD, but studies in the elderly suggest that group treatment using a behavioural-cognitive approach to change attitudes, as well as training with a physiotherapist, can help. The use of an assistive device and gait training can enlarge self-confidence. Instructions on how to stand up after a fall may also decrease fear of falling. An entirely different approach is required for cognitively impaired patients who can be overly confident and inappropriately ‘over-rate’ their own balance, resulting in risky behavior and falls. For them, restriction of hazardous activities might be the best solution to prevent recurrent falls. It is also important to inform the caregiver about activities that should be avoided.

Prevention of complications

Despite all efforts, most patients will continue to sustain at least occasional falls, and for patients with advanced PD the problem may become treatment-resistant. For this latter group, attention should increasingly be focused on preventing the complications of falls. For example, patients with PD can have a coexisting osteoporosis (caused by immobilization and perhaps endocrine disorders), that increase the risk of fracture. In PD patients presenting with a fracture, one should consider performing DEXA bone densitometry to establish whether osteoporosis is present. Treatment of osteoporosis may then reduce the risk of new fractures.

Who should be candidates?

It is necessary to identify patients who are most at risk of falling. Various factors are related to falling, but many are interrelated. Prior falls, disease severity (Hoehn and Yahr stage 3) and disease duration appear to be the most consistent predictors of falls. In a meta-analysis, the only independent predictor of falling was asking for earlier falls, and this is not a satisfactory predictor because patients have already begun falling. Less robust, but potentially interesting, predictors of falls were fear of falling, avoiding activities because of this fear, and presence of prior near-falls. This may offer a way to identify eligible candidates for fall prevention, even before the very first real fall has occurred.
One size fits all?

For clinicians, this is a familiar problem in clinical practice. The good part of the falls prevention approach, as described above, is its comprehensive character: this minimizes the risk of “missing” relevant risk factors, and theoretically provides the most aggressive and complete “gunshot” approach of the falling problem. But there are also less attractive sides of the coin. Being comprehensive, the entire program is costly, and importantly, it may be excessive for patients where a single factor is obviously responsible for the falling problem. For example, when patients exclusively fall while tripping over one particular rug in the living room, simply removing this rug may treat the problem and obviate the need for the remainder of the comprehensive falls prevention program. Alternatively, when patients fall because of syncope, is it necessary to pay a home visit and eliminate domestic risk factors for tripping? There is no evidence to support any particular strategy, but a practical compromise may be the following. When patients consistently display a

Fig 3 Diagnostic algorithm to classify the main types of falls in patients with a hypokinetic–rigid syndrome, modified after Voermans et al.*** The main categories of falls are shown in gray boxes. TLOC = transient loss of consciousness. ** When patients claim to fall spontaneously, this is usually caused by either freezing of gait (that is not recognized as such by the patient), or transient loss of consciousness (which is often incorrectly denied by elderly patients). b Although there is only little supportive literature††, it has been our impression that vertigo – in particular that caused by benign position-dependent vertigo – is not rare in patients with PD, perhaps because their relative immobility promotes development of debris in the semicircular canals.
specific type of falls, where one obvious risk factor is consistently responsible for the falls, then simply tackling this single factor may suffice. Figure 3 shows the most common fall types, as well as a pragmatic approach to ascertain which specific type of falls is present. In other patients a comprehensive multifactorial approach is recommended.

**CONCLUSION**

This chapter underscores that gait disability, postural instability and falls are common and frequently devastating features of PD. We have reviewed the clinical features, mainly to provide a rational basis for a multifactorial falls prevention program. This approach includes identifying both generic and PD-specific risk factors, in order to define a multidisciplinary and multifactorial intervention program that is tailored to each individual patient. This program includes: optimizing dopaminergic medication; reducing the use of sedative drugs; physiotherapy to improve transfers, gait (including freezing), balance and balance confidence, physical activity and the use of assistive devices; occupational therapy (home visits to eliminate domestic hazards); and treatment of orthostatic hypotension, urinary incontinence and visual impairments. More research is needed to underpin the merits of the proposed multidisciplinary falls prevention program, and to evaluate its cost-effectiveness. We also need to develop better ways of finding those patients who are most at risk for falling.

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