Recent advances in the assessment and treatment of falls in Parkinson’s disease
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Introduction and context
Falls are both common and debilitating in patients with Parkinson’s disease (PD). They have devastating consequences for affected individuals, often leading to injuries, secondary immobility, and reduced quality of life. Survival is reduced once falls have occurred [1], although a recent report failed to identify a relationship between falls and mortality risk in PD [2]. Falls are also important for the public health system, as the costs associated with falls and fall-related injuries are enormous. A prospective 20-year follow-up of 136 patients with newly diagnosed PD confirmed the high prevalence of falls (87%) and resulting fractures (35%) [3].

For the management of falls in PD, it is important to appreciate the complex and multifactorial pathophysiology. Both balance deficits and gait disorders inherent to PD can obviously lead to falls. Environmental factors such as slippery floors, loose rugs, poor lighting, or inadequate footwear may also contribute. There is an increasing awareness that freezing of gait – a sudden and episodically occurring inability to generate effective forward stepping movements – is one of the leading causes of falls, presumably because patients are caught by surprise due to the often unexpected nature of freezing events [4,5]. Recent work has underscored the additional importance of cognitive impairment as a key factor contributing to both falls and freezing [6,7]; falls are an issue in demented patients in particular [8]. Possible explanations for this link include more prominent dopaminergic denervation of the caudate nucleus [9] or more generalized cholinergic dysfunction [10].

Preventing falls is generally perceived as being difficult, but is not impossible. Given the complex multifactorial nature of falls and the experience in elderly non-parkinsonian populations [11], a multidisciplinary approach appears preferable, but for patients with PD this strategy is not yet backed by scientific evidence. Crucial elements in the therapeutic approach include optimizing pharmacotherapy – increasing PD medication for dopa-sensitive signs, and stopping sedative drugs – and tailored physiotherapy, based on evidence-based practice guidelines.

Here, we highlight a few important new developments in this field.

Recent advances
Assessment of the patient with falls
Each patient deserves a careful and systematic approach to identify all contributing factors. The quest should not stop when one causative factor has been found because falls are typically multifactorial in origin.
A recent prospective study in 101 patients with early-stage PD assessed how various measures could predict falls [12]. The best prediction was reached by combining disease-specific measures (such as PD severity and freezing of gait severity) with balance measures (such as the occurrence of symptomatic orthostatic hypotension, the Tinetti total score, and the extent of postural anterior-posterior sway). However, even this combination attained a sensitivity and specificity for predicting falls of only around 80%. Including cognitive measures that are more specific may further improve these predictive scores [13], but this remains to be examined.

Particular emphasis should be placed on testing for freezing of gait – using a series of provoking tests, including rapid 360 degree turns on the spot [14] – and for frontal executive dysfunction [7]. Specific attention should be paid to fear of renewed falling as this is common in PD [15]. Fear of falling is not only a risk factor for renewed falls [16], it may also lead to secondary immobilization with all its related adverse consequences [17].

**Optimizing medication**

Most balance deficits are resistant to dopaminergic medication. However, gait problems – including freezing of gait – can improve with dopaminergic medication, although doses that are higher or more frequent than those typically needed to increase hand functioning may be required [18]. Recent work points to a possible role for cholinesterase inhibitors in the treatment of gait and balance deficits, both in PD [19,20] and in Alzheimer’s disease [21], given that many axial motor deficits may result from misbalance between central cholinergic and dopaminergic systems [10]. Sedative drugs should be stopped whenever possible.

**Stereotactic deep brain surgery**

It has become clear that stereotactic deep brain surgery should be reserved for patients whose gait and balance deficits are still levodopa-responsive pre-operatively. Several studies are comparing bilateral stimulation of two different targets, namely the subthalamic nucleus (STN) and the internal globus pallidus [22,23]. The initial results indicate that both approaches are effective in providing short-term relief of motor symptoms, but one study suggested internal globus pallidus stimulation may offer better long-term outcomes for gait and balance deficits [22]. This difference was not evident in the largest study, although falls after a 2-year follow-up tended to be more common after STN stimulation [23], but this requires more study. In particular, STN stimulation has been associated with a worsening of gait and balance deficits, not only in the immediate postoperative phase, but also several years after follow-up [22,24]. Adjusting the stimulation parameters (e.g., markedly lowering the stimulation frequency) may be helpful in such patients [25]. The pedunculopontine nucleus has been studied as a promising new target, specifically for gait and balance deficits, but so far the results have not been very impressive [26,27].

**Physiotherapy**

The evidence-based guidelines on physiotherapy for PD were recently updated [28], providing a menu of treatment modalities to improve mobility and reduce falls. Examples of evidence-based physiotherapy strategies include cueing techniques, cognitive movement strategies, and the use of exercise. Rhythmic auditory or visual cues can improve gait in PD, including freezing of gait [29,30]. New inventive cueing approaches include walking glasses with different patterns of visual and auditory stimulation [31] and mental singing while walking [32]. Another promising approach, especially for PD patients with freezing of gait, is the use of cycling, the skill for which can be remarkably preserved in some patients [33]. Evidence based mainly on the effects of cueing on laboratory measures of gait and balance remains; the challenge is to ascertain an enduring clinical improvement in daily life, including a reduction of falls. Fears that cues might worsen the tendency to fall – for example, by increasing overall mobility – have not been substantiated [29]. The same holds true for the effect of exercise. A systematic review concluded that exercise in patients with PD results in improvement in postural stability and balance task performance [34]. However, power and quality of exercise studies have hitherto been insufficient to make definitive recommendations. Future randomized controlled trials will look into the (cost) effectiveness of exercise to reduce falls [35,36].

There is a growing body of literature on the use of treadmill training for gait rehabilitation in patients with neurologic disorders in general and for patients with PD in particular. A recent Cochrane review concluded that treadmill training may help to improve gait akinesia in PD, but the effect on falls remains unclear [37]. It also remains uncertain how long any improvements induced by treadmill training may last.

Another interesting new development is the use of robotics, which can assist PD patients in making mediolateral anticipatory weight shifts in preparation for taking a step [38]. The initial results are promising, and such new techniques now need to be implemented in situations that are more realistic to evaluate the clinical merits of these techniques in relation to everyday gait performance and falls.
Delivering such specific physiotherapy interventions to patients with PD likely requires trained expert physiotherapists. A large cluster-randomized trial showed that a community-based professional network with trained expert physiotherapists improved the quality of physiotherapy care and reduced health care costs, but without health benefits for patients [39].

Implications for clinical practice
Asking about falls and their impact on daily functioning should be a standard part of the evaluation of patients with PD. While awaiting further evidence, neurologists should consider installing a multidisciplinary team approach to tackle the vexing problem of falls in patients with PD. Management involves a systematic search for risk factors for falling, and a subsequent multifactorial approach aimed at eliminating or alleviating all patient-related and environmental risk factors for falling. Apart from optimizing dopaminergic medication, cholinergic therapies are now beginning to enter the field of play as well. Fear of falling must be addressed, and immobilization must be avoided as long as independent movements can still be made reasonably safely. The multidisciplinary team should ideally consist of trained and experienced professionals who treat large numbers of patients. Using this integrated approach, the goal should be to at least reduce falls or perhaps prevent them altogether, restore mobility and independence, and thereby help to maintain the quality of life for patients with PD.

Abbreviations
PD, Parkinson’s disease; STN, subthalamic nucleus.

Competing interests
The authors declare that they have no competing interests.

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