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ORIGINAL COMMUNICATION

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Prospective assessment of falls in Parkinson's disease

Abstract We studied prospectively the epidemiology, clinical impact and prediction of falls in 59 moderately affected patients with Parkinson's disease (PD) (mean UPDRS motor score 31.5; mean age 61 years) and 55 controls (mean age 60 years). At baseline, balance and gait were evaluated extensively. The retropulsion test (response to sudden shoulder pull) was executed first unexpectedly and five more times following prior warning. All persons used standardised scoring forms to document their falls during six months. Thirty patients (50.8 %) and eight controls (14.5 %) fell at least once (relative risk [RR] 6.1; 95 % confidence interval [CI] 2.5–15.1, p < 0.001). Recurrent (≥ 2) falls occurred in 15 patients (25.4 %), but in only two controls (RR 9.0; 95 % CI 2.0–41.7; p=0.001). Recurrent falls were more common among persons taking benzodiazepines (RR 5.0; 95 % CI 1.6–15.5; p < 0.01). Sixty-two percent of the falls in patients caused soft tissue injuries, but no fractures occurred. A fear of future falls was common (45.8 % of patients) and was accompanied by restriction of daily activities (44.1 % of patients). Seventy percent of falls reported by patients were 'intrinsic' (due to patient-related factors), but falls in controls were mainly (50 %) 'extrinsic' (due to environmental factors). None of the baseline posture and gait variables predicted falls adequately. The first 'unexpected' retropulsion test was more often abnormal than all subsequent (predictable) tests. Irrespective of its method of execution, the retropulsion test did not predict falls. A combination of asking for prior falls, disease severity and the Romberg test yielded the best overall diagnostic utility (sensitivity 65 % and specificity 98 %). Recurrent fallers were best predicted by disease severity (RR for Hoehn and Yahr stage 3 was > 100; 95 % CI 3.1–585) and asking for prior falls (RR 5.0; 95 % CI 1.2–20.9). We conclude that falls are common and disabling, even in relatively early stage PD. Recurrent fallers were best predicted by disease severity and presence of prior falls. Strategies to prevent falls in PD should particularly focus at intrinsic (patient-related) factors, such as minimising the use of benzodiazepines.

Key words Parkinson's disease · Falls · Prospective · Epidemiology

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Introduction

Postural instability and falls are among the most incapacitating features of Parkinson's disease (PD) [1, 24]. The epidemiology of falls in PD remains largely unknown. Furthermore, prediction of falls is difficult. Because history taking is often unreliable [17], clinicians depend upon clinical tests to estimate falling risks. The 'retropulsion test' (also termed 'sternum push' or 'pull test') is commonly used to probe postural instability [26, 34], but this test can be criticised for several reasons [4].

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We therefore prospectively investigated falls in PD. Our goal was to clarify the epidemiology, circumstances and clinical impact of falls. We also examined what clinical test (including the retropulsion test) could predict falls in daily life. A more detailed account of the fall circumstances has been presented elsewhere [44].

Methods

Subjects

We studied 59 patients with idiopathic PD and 55 age-matched controls (Table 1). Subjects were eligible subjects if they were ambulant community residents (with or without walking aids) and able to follow simple instructions (Mini Mental State Examination [MMSE] ≥ 24). We included only patients who fullfilled the criteria for idiopathic PD as defined by the brain bank of the United Kingdom Parkinson's Disease Society [21] and who sustained a clear and lasting beneficial response to chronic treatment with levodopa and/or a dopamine agonist (see below for details of medication) [14]. Exclusion criteria were any other neurological disorders, and visual or orthopaedic problems that were sufficiently severe to interfere with balance. We asked all eligible patients who visited our outpatient department between May 1998 and July 1999 to participate (Fig. 1). Sixty-one patients consented to participate, but two of them were later excluded because they were lost to follow-up shortly after inclusion (one patient died, one patient could no longer be reached). Age and sex of the remaining 59 patients were comparable to the entire outpatient population. Thirty-eight healthy partners of the patients were chosen as controls because their domestic risk factors for falls are identical to those of the patients. This is important because domestic variables such as stairs and slippery floors are important risk factors for falls [41]. For the same reason, domestic variables of the remaining 17 controls (healthy acquaintances of the patients or the investigators) were matched to those of the patients. The exclusion criteria used for the patients also applied to the controls. Medication taken during the study included levodopa (50 patients), dopamine receptor agonists (36 patients), anticholinergics (seven patients), amantadine (30 patients), selegiline (six patients), tolcapone (one patient), atypical neuroleptics (six patients), antidepressants (five patients), benzodi-

Table 1 Baseline clinical characteristics. Data are displayed as mean ± standard deviation or as the number of persons, as well as the number of persons for which this information was available (percentage between parentheses).

	Patients (N = 59)	Controls (N = 55)	Significance
Demographics			
Age (years)	60.8 ± 9.7	59.6 ± 8.5	p = 0.51
Women	21/59 (35.6)	37/55 (67.3)	p = 0.001
Living with partner	48/59 (84.2)	50/55 (90.9)	p = 0.39
Stairs within the house	46/59 (78.0)	44/55 (80.0)	p = 0.82
(Partially) dependent for ADL	23/59 (39.0)	0/55 (0.0)	p < 0.001
Alcohol (units/day)	0.8 ± 1.0	1.3 ± 1.4	p = 0.03
Duration of disease (years)	7.1 ± 4.8	–	–
Fall questionnaire			
Number of prior falls (≤ 6 months)	2.1 ± 5.4	0.3 ± 0.5	p = 0.16
Fallers (≤ 6 months)	23/59 (39.0)	15/55 (27.3)	p = 0.23
Fear of falling	27/59 (45.8)	4/59 (7.4)	p < 0.001
Restriction of activities	26/59 (44.1)	6/54 (11.1)	p < 0.001
Problems with multiple tasks	31/54 (57.4)	3/48 (6.3)	p < 0.001
Walking aids	13/58 (22.4)	0/55 (0.0)	p < 0.001
Neurological examination			
Hoehn & Yahr stage	2.3 ± 0.7	–	–
UPDRS motor score	31.5 ± 11.0	0.8 ± 1.7	p < 0.001
UPDRS total score	48.3 ± 15.2	1.8 ± 2.1	p < 0.001
MMSE	28.1 ± 2.0	29.2 ± 1.2	p < 0.001
Gait and balance			
Tinetti balance score	3.9 ± 3.0	0.4 ± 0.7	p < 0.001
Tinetti gait score	2.7 ± 2.3	0.1 ± 0.3	p < 0.001
Tinetti total score	6.6 ± 4.8	0.4 ± 0.8	p < 0.001
Romberg test	3/58 (5.2 %)	0/55 (0 %)	p = 0.24
Orthostatic hypotension	7/35 (20 %)	3/30 (10 %)	p = 0.32
Tandem stance			
Eyes open	23/59 (39 %)	2/55 (3.6 %)	p < 0.001
Eyes closed	44/59 (74.6 %)	23/55 (41.8 %)	p = 0.001
Tandem gait	24/56 (42.9 %)	5/54 (9.3 %)	p < 0.001
Standing up	9/58 (15.5 %)	1/55 (1.8 %)	p = 0.02
Sitting down	19/53 (32.8 %)	0/55 (0 %)	p < 0.001
Turning around	36/58 (62.1 %)	2/55 (3.6 %)	p < 0.001
Reaching	1/39 (2.6 %)	0/35 (0 %)	p = 0.53
Picking up object from floor	3/39 (8.3 %)	0/35 (0 %)	p = 0.24
Stops walking when talking	7/58 (12.1 %)	0/55 (0 %)	p = 0.01

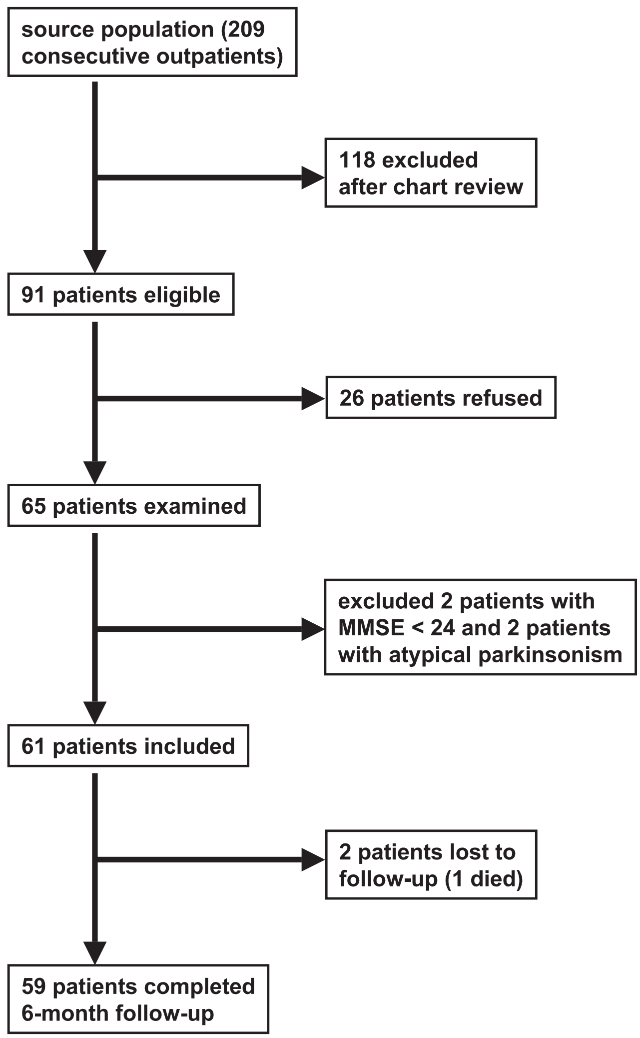

Fig. 1 Selection procedure for the patients.

azepines (16 patients and three controls) and antihypertensive drugs (nine patients and 10 controls). All subjects gave informed consent, as approved by the Ethical Committee of Leiden University Medical Centre.

Baseline clinical examination

The same investigator (BRB) examined all subjects (patients approximately one hour after intake of their usual medication). Baseline examination included a medical history, detailed evaluation of prior falls (using a standardised questionnaire) and a neurological examination, including the modified Hoehn and Yahr stages, the Unified Parkinson's Disease Rating Scale (UPDRS) [26] and the MMSE. Individual Hoehn & Yahr scores were stage 1 (N=5), stage 1.5 (N=5), stage 2 (N=19), stage 2.5 (N=11), stage 3 (N=18) and stage 4 (N=1). To reduce differences in answers due to e. g. education, the standardised questionnaire about falls was administered in the form of a personal interview. This was always performed in the presence of a partner, other close family member or carer, and these persons were asked to confirm the accuracy of all answers whenever possible. In addition, the standard questions were further clarified if patients misinterpreted our questions or volunteered ambiguities. The standardised interview included a description of living circumstances (alone or with partner / carer; presence of stairs yes/no), dependence (none, partial, or complete) in activities of daily living (ADL), accounts of recent falls (≤ 6 months), any fear of falling, any restrictions in daily activities because of this fear, and any problems with simultaneous performance of multiple tasks in daily life. Before asking about prior falls, we explained the definition of a fall as 'any unexpected event that caused the person to unintentionally land on any lower surface (object, floor, or ground), regardless of any sustained injury' [11, 25, 29]. We restricted the account of recent falls to a 6-month period to minimise the risk of recall bias [17]. The question about problems with simultaneous performance of multiple tasks in daily life was illustrated by two standard examples ("We will give you two examples. In the last six months, did you have more difficulty than previously to walk and talk to someone at the same time? Did you have more difficulty than previously to walk and carry something in your hands?"). These two examples were chosen because elderly persons and Parkinson patients are known to have difficulty with these tasks [6, 9, 27, 28]. We also posed an open question about problems with any other simultaneous tasks. Persons were regarded as fallers if they reported at least one previous fall in the preceding six months. Equilibrium and mobility were tested with Tinetti's Mobility Index [40], the normal Romberg test, the sharpened Romberg test (i. e. standing with eyes open and eyes closed, with the feet in tandem stance) [37], tandem gait (walking 10 steps with feet directly in front of each other), reaching for an object (standardised for each subject at a level just above the head) and bending forward to pick up an object from the floor. These additional tests were scored as either normal or abnormal. The 'Stops walking when talking' test [27] was also administered. The results of this test in the first 38 patients and 35 controls are briefly described elsewhere [5]. In 35 patients and 30 controls, blood pressure was measured in a recumbent position and after two minutes of standing. Orthostatic hypotension was defined as a drop in systolic blood pressure of more than 20 mm Hg or a drop in diastolic blood pressure of more than 10 mm Hg [32]. Specific attention was paid to the retropulsion test, which is commonly used to probe postural disturbances in PD [26]. Despite widespread clinical use, it remains unclear how the retropulsion test should be executed. The patient can be warned verbally or prepared by practice [26, 39, 42], but some authors claim that the first and most unexpected test is most informative [4, 34]. We therefore assessed several variants of the retropulsion test to identify the best predictive version. The test consisted of a sudden and unexpected shoulder pull, performed by an examiner standing behind the person [4, 26]. In all subjects, the test was executed the first time without any warning. Directly thereafter, the retropulsion test was repeated with prior warning. In 39 patients and 35 controls, the test was repeated four additional times with prior warning to study habituation effects [8]. The amount of retropulsion was scored as described by the Parkinson's Study Group [26]. In addition, we counted the number of backward steps needed to restore balance.

Prospective assessment of falls

Both patients and controls were instructed to directly document the circumstances and consequences (injuries or fear) of all falls for six months, using standardised scoring forms. Subjects were asked to describe the fall in their own words, and to tick pre-specified options regarding the environment where the fall occurred (indoors or outdoors), the specific activity at the time of the fall and any complaints that preceded the fall. Subjects were also asked to tick whether they performed multiple tasks simultaneously at the time of the fall. Patients recorded the effect of their antiparkinson medication at the time of the fall, by ticking one of the three following options: (a) insufficient effect, very stiff and slow; (b) good effect, not very stiff and slow; or (c) good effect, but excessive involuntary movements ('dyskinesias'). Persons were carefully instructed to return these scoring forms by mail directly after each fall. In addition, persons were contacted by telephone every two weeks to assure that all falls were documented.

Persons were classified as a 'faller' if they suffered at least one fall, whereas 'recurrent fallers' had at least two falls. 'Injurious fallers' were persons who sustained fractures or soft tissue injuries (including bruises, skin lacerations, haematomas and joint dislocations) after at least one fall. Finally, persons were defined as 'serious fallers' if their falls were recurrent (≥ 2), injurious, or both. This variable encompasses all clinically relevant falls. Recurrent falls are a better index of chronic disorders than single falls, which are often caused by environmental accidents with a low recurrence rate [33] and therefore have little clinical importance, unless injury occurs.

Based upon the answers to the scoring forms, we scored a fall as 'extrinsic' if it was caused by an environmental cause (e. g. collisions), as 'intrinsic' if it was caused by mobility or balance disorders, misperception of the environment or loss of consciousness, and as 'non-bipedal' if it occurred while the person was not in a bipedal stance (e. g. fall from a chair) [25]. Falls were also categorised as 'base of support falls' (e. g. trips or slips), 'centre of mass falls', either self-induced (e. g. bending, reaching or turning) or externally applied (e. g. a push or collision), or as falls in which there was no obvious perturbation (with or without loss of consciousness) [29]. The remaining falls were labelled as 'unclassified'.

Statistical analyses

Baseline variables were compared between patients and controls using the unpaired *t* test, the chi square test and Fisher's exact test, with a p-value of 0.01 as a Bonferroni-type correction. Duration of the disease was compared between fallers and non-fallers using the unpaired *t* test. The recurrent fallers of both groups will be reported as the primary outcome measure. However, very similar results were obtained when single, serious or injurious falls were used as the primary outcome variable, and when patients were analysed separately. The sensitivity and specificity for prediction of recurrent falls were calculated for all baseline variables. In addition, stepwise forward logistic regression analysis was performed to evaluate which combination of variables best predicted recurrent falls. In this model, we successively entered variables from the baseline history (age, sex, alcohol use, dependence in ADL, disease duration), the prior fall history (faller status, fear of falls, restriction of activities, problems with multiple tasks, use of walking aids), the general physical examination (Hoehn and Yahr stages, UPDRS score) and, finally, the balance and gait examination (Tinetti score and the additionally recorded measures).

Results

Baseline assessment (Table 1)

There were more women among controls than among patients (a consequence of our choice for partners, rather than sex-matched persons, as controls). Domestic variables (as exemplified in Table 1 by the proportions of subjects that lived together with a partner, and by the proportions of subjects with stairs within the house) did not differ between patients and controls. Patients were more often dependent for ADL than controls. The MMSE of patients was slightly but significantly lower than in controls, but owing to our inclusion criteria, none of the patients had obvious cognitive impairment.

The average number of prior falls and the proportion of self-reported fallers (≥ 1 fall) during the six previous months were somewhat higher for patients than controls, but these differences were not significant. Almost 50 % of patients expressed a fear of falling. A restriction of daily activities because of this fear was also more common among patients than controls. Furthermore, many patients reported difficulties with simultaneous performance of multiple tasks, such as walking and carrying a tray.

Patients performed worse than controls on most tests of balance and gait (Table 1). Tandem stance with eyes closed was most often abnormal in patients, but also in about 42 % of the controls. Balance while turning and tandem gait were also sensitive measures of PD, and these tests were rarely abnormal in controls. Several other measures, such as the Romberg test and orthostatic hypotension, did not differ between patients and controls. The 'Stops walking when talking test' was abnormal in only seven patients, and in none of the controls.

The responses to the six consecutive retropulsion tests are shown in Fig. 2. The first retropulsion test (i. e. without prior warning) was abnormal (UPDRS score ≥ 1) in 10 patients (16.9 %) and six controls (10.9 %; p = 0.55). Only three patients and one control had to be caught by the examiner (UPDRS score = 2). No person had a spontaneous tendency to fall (UPDRS score = 3). Most corrective steps were taken after the first unexpected shoulder pull by both patients (1.6 ± 1.3) and controls (1.6 ± 1.2; p = 0.81). Overall, for subjects who received six consecutive retropulsion tests, test abnormality decreased with warning and repetition in patients and controls (p < 0.001), both for the UPDRS score and the number of corrective steps taken. These warning and learning effects did not differ between both groups (p = 0.47). The warning and learning effects were largely attributable to the second test, which was performed better than the first test in both groups. No relevant further improvement was noted for the remaining retropulsion tests (no difference between the second and sixth test in both groups; p = 0.30). None of the retropulsion tests discriminated well between patients and controls.

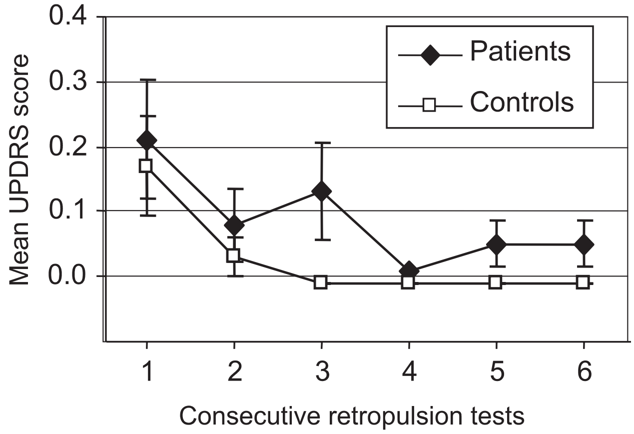

Fig. 2 Responses to the six consecutive retropulsion tests for patients and controls. The UPDRS-score is used as outcome measure. Similar results were obtained for the number of corrective steps.

Prospective follow-up (Table 2)

During the six-month follow-up, patients reported 205 falls, whereas controls reported only 10 falls. The period between baseline examination and the first fall was somewhat shorter for patients than controls, but this difference was not significant. However, the mean (± standard deviation) period between baseline examination and the first fall was significantly shorter for persons who sustained recurrent falls (1.0 ± 1.0 month) than for persons with maximally one fall (2.9 ± 1.8 month) (p < 0.005). Among patients, the proportion of prospectively identified fallers (50.8 %) tended to exceed the self-reported estimate during the six previous months (39 %; p = 0.27). In contrast, fewer controls tended to fall during follow-up (14.5 %) than during the previous six months (27.3 %; p = 0.16). The proportion of persons that reported at least one fall was much higher for patients than controls (relative risk [RR] 6.1; 95 % confidence interval [CI] 2.5–15.1; p < 0.001). The proportion of persons who fell more than once during follow-up was also higher for patients. One quarter of patients had recurrent (≥ 2) falls, as opposed to only two controls (RR 9.0; 95 % CI 2.0–41.7; p = 0.001).

Complete documentation about circumstances of falls was available for 150 falls of patients and all 10 falls of controls (Table 2). Information about the falls could not be obtained reliably for 55 falls of the patients (usually due to poorly legible handwriting; a few falls were only detected during the reminding telephone calls, but details of these falls were not included to avoid any recall problems). Patients fell mostly indoors, whereas controls usually fell outdoors. Patients mostly suffered

Table 2 Fall rates, circumstances and consequences of falls.

	Patients (N = 59)	Controls (N = 55)	Significance
Fall rates			
Time to first fall (months)	1.7 ± 1.7	2.5 ± 2.0	p = 0.35
Fallers (≥ 1 fall)	30 (50.8 %)	8 (14.5 %)	p < 0.001
Recurrent fallers (≥ 2 fall)	15 (25.4 %)	2 (3.6 %)	p = 0.001
Characteristics[a]			
Falls indoors	124 (82.7 %)	2 (20 %)	p < 0.001
Lach classification (25)			
Intrinsic falls	105 (70 %)	4 (40 %)	p = 0.02
Extrinsic falls	20 (13.3 %)	5 (50 %)	
Non-bipedal falls	2 (1.3 %)	0 (0 %)	
Non-classifiable falls	23 (15.3 %)	1 (10 %)	
Maki classification (29)			
Base of support falls	21 (14 %)	5 (50 %)	p = 0.02
Centre of mass falls	108 (72 %)	4 (40 %)	
No obvious perturbation falls	8 (5.3 %)	0 (0 %)	
Non-classifiable falls	13 (8.7 %)	1 (10 %)	
Clinical condition			
Poorly controlled	44 (29.3 %)	–	–
Well controlled (no dyskinesias)	54 (36 %)	–	–
Well controlled (with dyskinesias)	52 (34.7 %)	–	–
Consequences			
Injurious fallers	15 (25.4 %)	6 (10.9 %)	p = 0.06
Serious fallers[b]	21 (35.6 %)	6 (10.9 %)	p < 0.005
Number of falls with:[a]			
Injury	93 (62 %)	7 (70 %)	p = 0.74
Inability to get up	37 (24.7 %)	3 (30 %)	p = 0.71
(More) fear of future falls	63 (42 %)	1 (10 %)	p = 0.05

Data are displayed as mean ± standard deviation or as individual counts (percentage between parentheses) with an abnormal test result.
[a] Complete documentation available for 150 falls of patients and all 10 falls of controls
[b] persons with recurrent falls, injurious falls, or both.

intrinsic falls, whereas environmental hazards (extrinsic falls) caused most falls in controls. 'Centre of mass falls' predominated among patients, whereas controls had more 'base of support falls'. Centre of mass falls among patients occurred most commonly while turning around (24 % of the 150 falls), standing up (15 %) and bending forward (16 %). About one third of falls occurred when patients rated their symptoms as poorly controlled. About two-thirds of all falls by patients occurred when they rated their symptoms as well controlled, although concurrent dyskinesias were present in half of them. Six falls were related to sudden freezing, all when symptoms were poorly controlled. Only one fall was preceded by sudden loss of consciousness.

The proportion of injurious *fallers* tended to be highest among patients, but the proportion of injurious *falls* did not differ between both groups (Table 2). Among those persons who fell at least once, the proportion of injurious fallers tended to be even higher for controls (six out of eight fallers or 75 %) than for patients (15 out of 30 fallers or 50 %; p = 0.26). Serious fallers (recurrent, injurious, or both) were more common among patients than controls. No fractures or life-threatening complications occurred, but soft tissue injuries were very common. An inability to get up after a fall occurred in both patients and controls, and several patients lay on the floor for hours. In addition, falls often induced or aggravated a fear of future falls that led patients to further restrict their activities.

Prediction of falls (Table 3)

Of the questionnaire items, asking for earlier falls attained the best sensitivity (76.5 %) with a comparable specificity (74.2 %) in identifying recurrent fallers. Asking for problems with multiple tasks also had a reasonable sensitivity and specificity. Overall, the proportion of women did not differ between recurrent fallers (9/17;

Table 3 Prediction of recurrent fallers (pooled results of patients and controls). Non-fallers included persons without any falls or a single fall. Data are displayed as mean ± standard deviation or as individual counts (the percentage shown between parentheses for fallers denotes the sensitivity; the percentage shown for non-fallers is equivalent to 100 % minus the specificity). Abnormal retropulsion tests shown here include all UPDRS scores ≥ 1, but statistical analyses were performed using the actual scores. Only variables that differed (p < 0.01) between recurrent fallers and non-fallers are displayed, plus several pertinent variables that did not discriminate well between both groups.

	Recurrent fallers (N = 17)	Non-recurrent fallers (N = 97)	Significance
Fall questionnaire			
Fallers (≤ 6 months)	13 (76.5)	25 (25.8)	p < 0.001
Fear of falling[a]	9 (52.9)	22 (22.9)	p = 0.02
Problems with multiple tasks[b]	11 (73.3)	23 (26.4)	p = 0.001
Use of walking aids[a]	6 (35.3)	7 (7.3)	p < 0.005
Neurological examination			
Hoehn & Yahr stage	2.8 ± 0.6	2.1 ± 0.6	p < 0.001
UPDRS motor score	34.8 ± 12.5	17.1 ± 16.6	p < 0.001
UPDRS total score	52.8 ± 17.9	26.5 ± 24.7	p < 0.001
MMSE	27.8 ± 2.2	28.7 ± 1.6	p = 0.13
Gait and balance			
Tinetti balance score	5.1 ± 2.8	1.7 ± 2.5	p < 0.001
Tinetti gait score	3.8 ± 2.4	1.0 ± 1.8	p < 0.001
Tinetti total score	8.9 ± 4.6	2.7 ± 4.0	p < 0.001
Retropulsion tests			
First	5 (29.4)	11 (11.3)	p = 0.07
Second	1 (5.9)	2 (2.1)	p = 0.05
Tandem stance			
Eyes open	9 (52.9)	16 (16.5)	p < 0.005
Eyes closed	15 (88.2)	52 (53.6)	p < 0.01
Romberg test[a]	3 (17.6)	0 (0.0)	p < 0.005
Sitting down[a]	8 (47.1)	11 (11.5)	p = 0.001
Turning around[a]	12 (70.6)	26 (27.1)	p = 0.001
Tandem gait[c]	10 (62.5)	19 (20.2)	p = 0.001
Stops walking when talking	2 (12.5)	5 (5.2)	p = 0.26

[a] Data were unavailable for one non-faller,
[b] two fallers and 10 non-fallers,
[c] one faller and three non-fallers,
[d] one faller.

52.9 %) and persons with maximally one fall (49/97; 50.5 %). However, all eight fallers among our controls were women, whereas men (n=8) and women (n=7) were equally distributed among the recurrent fallers in the patient group. Recurrent falls were more common in more severely affected patients and persons with higher scores on the Tinetti Mobility Index. Among patients, fallers had a somewhat longer duration of the disease than non-fallers, but this difference was not significant. For example, disease duration was 8.5 ± 4.6 years among patients with recurrent falls, compared with 6.6 ± 4.8 years among patients without recurrent falls ($p = 0.18$). The MMSE was only slightly lower among recurrent fallers, but this difference was not significant.

Benzodiazepines were used more often by patients (n = 16; 27.1 %) than by controls (n = 3; 5.5 %) (Fisher's exact test, $p < 0.005$). Recurrent falls were reported by 36.8 % (7/19) of persons using benzodiazepines, and by 10.5 % (10/95) of persons not using benzodiazepines (RR 5.0; 95 % CI 1.6–15.5; $p < 0.01$).

Most balance and gait tests predicted falls insufficiently. This included the retropulsion test (irrespective of how it was executed or scored), which had a good specificity, but a very low sensitivity. The area under the receiver-operating curve (calculated for the average of all six retropulsion tests) was 0.62 (standard error 0.07), reflecting an insufficient sensitivity and specificity to predict falls. Tandem stance with eyes closed, turning around and tandem gait had a moderate to good sensitivity, but the specificity was only acceptable for tandem gait (79.8 %) and turning around (72.9 %). The proportion of persons with orthostatic hypotension did not differ significantly between recurrent fallers (23.1 %) and non-fallers (13.5 %; $p = 0.41$). The 'Stops walking when talking' test was rarely abnormal in recurrent fallers.

The logistic regression analysis has to be interpreted with some caution given the relatively small sample size. When all variables were entered into the logistic regression model simultaneously, the combination of asking for prior falls, disease severity and the Romberg test yielded the best overall diagnostic utility (sensitivity 65 % and specificity 98 %). However, the added benefit of the Romberg test was limited for practical purposes because this test was impaired in only three recurrent fallers (and in none of the remaining subjects). In contrast, disease severity (as indexed by the Hoehn and Yahr scores) was helpful in identifying subjects at risk for recurrent falls. Thus, the RR of recurrent falls was 13.4 (95 % CI 0.4–27) for patients with Hoehn and Yahr stage 1 to 2.5, and > 100 (95 % CI 3.1–585) for the most severely affected patients (who were all but one in Hoehn and Yahr stage 3). Asking for prior falls in the previous 6 months was also helpful in identifying subjects at risk for recurrent falls (RR 5.0, 95 % CI 1.2–20.9). Identical results were obtained when the prediction model was applied to patients only, and when patients and controls were pooled (where controls were given a Hoehn and Yahr score of 0 and disease duration of 0 years).

Discussion

The first important conclusion is that falls are very common, even relatively early in the course of PD. More than 200 falls occurred in 59 patients during six months, 50 % of the patients fell at least once, and about 35 % suffered recurrent or injurious falls. Comparable fall rates emerged from an uncontrolled study where 59 % of Parkinson patients fell at least once during three months [19]. In contrast to the latter study, we also investigated falls in healthy controls, which permitted us to estimate relative risks for falls. Thus, Parkinson patients had a nine-fold increased risk of sustaining recurrent falls. These prospectively determined fall rates exceed those of retrospective studies [23, 31, 35, 36] (and the retrospective estimate in this study), perhaps because merely asking for falls underestimates the true incidence [17]. An 'amnesia for falls' may well occur in PD patients who are often cognitively impaired [18, 30]. Indeed, patients had a lower MMSE than controls, and elaborate tests might have unveiled more cognitive decline. Another possibility is that concurrent disease progression during the study explained why the prospectively obtained fall rate in our patients exceeded their own retrospective estimate.

The fall rates for patients well exceeded those of controls, despite the female preponderance in controls. This sex difference was a consequence of our choice for partners as controls, which we considered important because domestic variables such as stairs and slippery floors are important risk factors for falls [41]. This advantage outweighed the resultant sex difference between patients and controls. In fact, the actual difference between patients and controls is perhaps even greater than in this study because women fall more often than men [41]. Indeed, all eight fallers among our controls were women.

Our analysis of fall circumstances is the second important result, as this could form the basis for potential preventive measures. PD patients usually fell indoors, suggesting that reduction of domestic hazards could be fruitful. However, this approach may eliminate only a minority of falls, because patients often fell unrelated to environmental hazards (they had a high proportion of 'intrinsic' falls). Indeed, patients commonly had centre of mass falls (most often while turning around), which again suggests that the underlying balance disorder caused most falls. Apparently, antiparkinson medication did not reduce these balance problems, because two-thirds of falls occurred when patients considered their symptoms to be well controlled. Other studies also suggest that postural instability in PD is resistant to conventional pharmacotherapy [3, 10, 22, 23]. In fact, treatment may paradoxically aggravate falls because amelioration of other symptoms improves mobility (and thus increases the risk of falling) [38], without improving balance. Furthermore, our results suggest that drug-induced dyskinesias may contribute to some of the falls [35]. However, more detailed research is needed here because we did not quantify the severity and daytime duration of dyskinesias. Certainly, development of improved therapeutic strategies to reduce postural instability is needed. One important measure that could already be taken is reduction of benzodiazepines, which were commonly used by our patients. Similar to other studies [13, 16], we found that use of benzodiazepines was associated with a five-fold increase in the risk of recurrent falls.

A third important finding was the high rate of adverse consequences of falls. No fractures occurred, but soft tissue injuries were very common. The proportion of injurious fallers was slightly higher in controls than in patients, possibly because patients fell mostly indoors where soft carpets may have absorbed the impact of their falls. In addition, patients may suffer more 'low-energy' falls because they walk more slowly or fall from a low height, for example while reaching for objects on the floor. This differs from healthy persons who rarely fall, but if they do, it is usually due to overwhelming external causes that often induce injuries.

A commonly overlooked, yet incapacitating consequence of falls is a fear of future falls, which was common among patients. This fear of falls forced patients to restrict their physical activities and sometimes led to social isolation. This restriction of activities perhaps explains the high proportion of indoor falls in our patients. The immobilisation and reduced ability to participate in social life are as important as falling itself in reducing the quality of life for PD patients [7]. Immobilisation also underlies the complex relation between falls and disease duration, which only tended to be longer in fallers compared to non-fallers. We suspect that falls are most common in relatively early stage PD (as was the case in our patients), when postural instability develops and patients are sufficiently mobile to be actually at risk for falls [7]. Indeed, in our study, fall risks were highest for patients with Hoehn and Yahr stage 3 PD. As the disease progresses further, both postural instability and the fear of falls worsen, causing patients to become increasingly immobilised. In effect, this 'prevents' additional falls and obscures the relation between falls and disease duration [7].

The fourth aspect of our study related to prediction of falls. Recurrent fallers were best predicted by a combination of asking for prior falls, disease severity and the Romberg test. Although the specificity of this combination was excellent (98 %), the overall diagnostic utility was somewhat limited by the moderate sensitivity (65 %), indicating that a substantial proportion of recurrent fallers would be misclassified as non-fallers. Because of the grave consequences of falls and the emerging possibilities for therapeutic intervention [7, 12, 15], a test with a higher sensitivity (perhaps at the cost of a lower specificity) would be preferable. Presently, the best predictors of falls were disease severity and asking for prior falls. For example, the risk of recurrent falls was increased five-fold in persons with earlier falls. The moderate sensitivity is perhaps explained by the amnesia for falls mentioned previously.

Interestingly, none of the commonly used clinical tests of balance and gait could predict falls adequately. This included the retropulsion test, which is commonly used to document balance impairment in PD. The retropulsion test has several theoretical shortcomings, and how this test should be executed is debated [4, 7]. The response to the first shoulder pull is presumably most informative (certainly when given without prior notice) because this best resembles the unexpected falls that occur in daily life. Because patients adapt to the test [34] learning effects (that are not operative in daily life) could confound subsequent shoulder pulls. The first retropulsion test is also preferable because PD patients cannot cope with unexpected external perturbations [37]. Indeed, the first and unexpected shoulder pull yielded different results (more corrective steps and a higher UPDRS-score) than all subsequent tests, which produced largely similar results. Both the prior warning signal and learning effects may explain the better performance for the second to sixth retropulsion tests. However, none of the six retropulsion tests discriminated well between patients and controls, and all tests predicted falls poorly. This predictive capability was perhaps insufficient because our patients were relatively mildly affected (even the first and unexpected retropulsion test was normal in most patients). Yet, this moderately affected group is interesting because the added benefit of a screening test for falls would be greatest. We therefore conclude that the retropulsion test is not suitable for early detection of fallers. Perhaps the test is more useful in later stages of PD to rate the severity of balance impairment.

Assessment after overnight withdrawal of levodopa might predict falls better than the present scores. However, major differences are unlikely because most falls occurred when symptoms were well controlled. Furthermore, scores for postural instability usually change little with dopaminergic medication [3, 10, 22, 23].

A potential shortcoming of our study was created by the inclusion of outpatients attending a university hospital with an interest in movement disorders. This selection bias might preclude extrapolation of our findings to the more general population of patients with PD, for example because relatively severely affected patients are more likely to visit specialised outpatient clinics. However, this possible selection bias by disease severity appeared negligible in our study because we excluded patients with severe signs (inability to walk without assistance, MMSE < 24). Indeed, the average UPDRS motor score of our patients was 31.5 and none of them had a Hoehn and Yahr score of 4. Such patients are also commonly seen in outpatient clinics outside specialised university centres. We also reduced the risk of including patients with atypical hypokinetic-rigid syndromes (who fall more frequently and earlier in the course of the disease [43] by using the inclusion criteria for idiopathic PD as defined by the brain bank of the United Kingdom Parkinson's Disease Society [21]. In addition, all patients responded well to chronic treatment with antiparkinson medication, which always included levodopa and/or a dopamine agonist [14].

We cannot entirely exclude that our study was underpowered to detect variables with a modest ability to detect falls. However, most comparisons between prospectively determined fallers and non-fallers were highly significant, which generally does not suggest insufficient power. Although the number of subjects was relatively small, the incidence of falls was very high. Furthermore, the observed sensitivities were consistently low to moderate. A larger sample size may have helped to reduce the uncertainty surrounding these sensitivities and attain statistical significance, but it is unlikely that very different sensitivities would have been obtained. Certainly, further studies in larger patient groups remain necessary. Such studies should also include tests with a 'multiple task' design (simultaneous assessment of different aspects of postural control) as these may predict falls better than simple tests of isolated postural components [27]. This may be particularly true in PD where the pathophysiology of postural instability is multifactorial [2, 3, 20] . Indeed, during the standardised interview, 57 % of our patients reported difficulties with executing simultaneous tasks, such as carrying a tray or talking while walking. Although these answers may be subject to interindividual variability (*e. g.* due to differences in education) and recall bias [17], it was interesting that very comparable results emerged from the more reliable prospective survey where multiple-task performance played a role in about 50 % of the falls (see reference (44) for details). In the present study, we also corroborated our earlier report [5] in a smaller patient group that simple dual-task performance, such as the 'Stops walking when talking' test [27], is rarely abnormal in PD, perhaps because this test is only abnormal in cognitively impaired patients [5]. However, preliminary results suggest that simultaneous or sequential performance of truly multiple (up to eight) tasks can discriminate much better between PD patients and controls, even in relatively early stages of the disease [6]. We are now prospectively investigating whether this 'Multiple Task Test' can also predict actual falls in daily life.

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