Falls in Parkinson Disease
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Abstract
Falls are a major risk for Parkinson disease patients (PD). We sought to understand why patients fall. In one study we followed 404 PD patients for a year, 204 of who fell at least once. We did not distinguish between single and recurrent fallers. In a second study we followed 249 different patients for a year, 206 of whom fell once and 44 fell more than once (recurrent fallers).

In the first study fallers were significantly older, 72.6 ± 5.8 versus 66.9 ± 6.1 years, had PD significantly longer 9.3 ± 3.4 versus 5.4 ± 2.2 years, had significantly higher (worse) motor Movement Disorder Society (MDS) Unified Parkinson Disease Rating Scale (UPDRS) scores 29.3 ± 10.9 versus 18.9 ± 8.3. Fallers walked with significantly shorter steps: 0.45 ± 0.09 versus 0.60 ± 0.13 m. Assessing step length, a simple “bedside” test, was a useful aid in predicting who might fall.

In the second study recurrent fallers had PD significantly longer, 12.6 ± 7.0 versus 5.9 ± 4.5 years, had significantly higher motor MDS UPDRS scores 31.2 ± 12.7 versus 19.7 ± 8.3 and walked with significantly shorter steps: 0.37 ± 0.18 m versus 0.52 ± 0.19 m. A major difference between recurrent and single fallers was an inability of recurrent fallers to stand on one leg for <3 s: 95% versus 11%, odd ratio 178 CI 95% 39.5-801.2 Single fallers who are unable to stand on one leg for <3 s are at risk for recurrent falls.

The short step, we believe, is an adaptation to postural instability, inability to maintain an upright position. The inability to stand on one leg, by depriving the patient of roughly half their proprioception, is a measure of risk for falls. Parkinson disease is viewed as a motor disorder, but impaired proprioception, a sensory symptom, is a major cause of recurrent falls.

Keywords: Parkinson disease; Falls; Freezing of gait

Introduction
Falls are a major cause of disability in Parkinson disease (PD) [1,2]. In a study of 761 hospital admissions for PD only 15% were for management of PD, while 39% were for falls [1]. A major risk for recurrent falls is a previous history of a fall. PD patients who fall once may do so because of PD or because of factors such as poor eye-sight, leg weakness and environmental hazards [3,4].

There is variability in the reported prevalence of falls in PD: from 11% to 68% [3-14]. The variability depends on whether specific fall risk factors are excluded. These include visual loss, orthostatic hypotension resulting from anti-hypertensives or imbalance resulting from tranquilizers, sedatives, or alcohol. The variability in reporting also depends upon whether only serious falls (requiring medical attention) or non-serious falls were recorded [3-14]. The variability also includes whether persons with evolving atypical Parkinson disorders such as Progressive Supranuclear Palsy (PSP) or Multiple System Atrophy (MSA) persons but with a high predilection to fall were excluded [6].

Methods
In 2010-2011 we saw 460 PD patients [3]. We excluded patients with atypical Parkinson disorders. We excluded patients with PD and dementia, Mini-Mental Status Examinations, MMSE, <24. We excluded patients who were legally blind. We excluded patients with orthostatic hypotension. Although orthostatic hypotension can be part of PD, it can also result from the use of anti-hypertensives, diuretics or dehydration [15,16]. As we often could not distinguish between them we excluded such patients. We excluded patients with neuropathy when it resulted in impaired proprioception or weakness. We excluded patients with major orthopedic problems [13,14]. The number of excluded patients was 56.

We analyzed 404 PD patients: 214 males, 190 females. All were examined every 4 months as part of their routine office visit. At each visit patients and care-givers were instructed to call us if they fell. Of the 404 persons with PD, 204, 50.5%, fell: 164 (80%) patients fell once, 41 fell (20%) more than once. We compared fallers with non-fallers.

We analyzed serious falls where all 4 limbs, the skull or buttocks hit the ground, with patients sustaining a fracture or soft tissue injury. All patients were examined using the motor MDS UPDRS [17] and selected subtests. All patients were studied using the BNI balance scale [18]. This included the ability of a patient to stand on one leg for at least 3 s. All patients walked 7.63 m (25 feet). Adjustments were made for height, the number of steps taken was counted, divided by 7.63 m and an average was obtained.

Next we did a second study 2011-2012 [19]. None of the patients were participants in the first study.

We analyzed 205 patients: 113 men, 92 women of whom 161 (79%) fell once and 44 (21%) fell more than once. All patients were informed that the information collected could be used for research but that they personally could not be identified. Approval for the analysis

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was obtained by the St. Joseph's Hospital institutional review board. No patients were compensated. As the evaluations were part of the patient's routine care no special consent other than the standard signed consent obtained from all patients at the time their visit was obtained. Continuous variables were analyzed using t-tests and categorical variables were analyzed using chi-square tests. We used the SAS 8.01 statistical software package. The first study was analyzed separately from the second study.

Results

In the first study of 404 PD patients, 50.5% fell (204). Among the fallers, 112 (54%) were males, 92 were females (46%). Among the non-fallers 112 (56%) were males, 88 (44%) were females. Among the 204 fallers, 41 (20%) fell more than once. In this study we only looked at fallers (single and recurrent) versus non-fallers. Age, duration of PD, MDS UPDRS motor scores were significantly higher (worse) in the fallers (Table 1). Step length was significantly shorter (Table 1). There were no differences in BNI subtests of One Legged Stance or Turning. Among fallers 43 patients, 21.3% had FOG, 161 (78.9%) did not. Among non-fallers 21 patients, 10.5% had FOG, 179 patients, 89.5% did not. Fallers were more likely to have FOG than non-fallers: Odds Ratio 2.28, 95% CI 1.30-3.99, P<0.0042.

Among fallers 84% were on levodopa, among non-fallers 80% were on levodopa. Forty percent of fallers and 29% of non-fallers had dyskinesias. Although a higher percent of fallers had dyskinesias we cannot comment on the contribution of dyskinesias to falls because we recorded only the presence, not the severity of dyskinesias.

In the second study, 205 PD patients fell, 44 of who fell at least twice. PD duration and MDS UPDRS Motor Score were significantly higher in recurrent fallers (Table 2). Step length was significantly shorter (Table 2). MDS UPDRS sub-tests of Gait, Pull and FOG were significantly worse and One Legged Stance and Turning sub-tests were significantly worse in recurrent fallers (Table 1 and 2). Sub-tests of Postural Stability including One Legged Stance and Pull sub-test were worse than sub-tests of Locomotion including Gait sub-test and step length.

Among single fallers 87.5% were on levodopa, among recurrent fallers 100% were on levodopa. 40% of single fallers had dyskinesias, 56% of recurrent fallers had dyskinesias.

Discussion

The prevalence of falls, at least 50%, in both studies is comparable to that reported by others [4-10]. It's estimated that 33% of all people over age 65 years fall at least once a year. The costs associated with fall-related injuries are high and estimated to reach $30 billion by 2020 by the Rand Corporation [20]. These figures are likely to be higher in PD, because a higher percent of people with PD fall and are more likely to fall repeatedly. If falls, and especially recurrent falls, can be reduced in PD, they possibly can be reduced in the elderly [20-24].

Fallers have PD longer and are more disabled. However, in an individual patient who falls, the duration of PD may be insufficient to predict another fall. And in an individual patient the MDS UPDRS motor score may be insufficient to predict another fall. This is because the MDS UPDRS is weighted toward upper extremity rigidity, tremor and bradykinesia, metrics that are less likely to predict falls.

Fallers take significantly shorter steps. This in our opinion is an adaptation to impaired postural stability. Freezing of gait, the “ultimate short step”, may be an extreme example of such an adaptation [24,25].

Recurrent fallers in the second study were significantly more likely to be unable to stand on one foot for <3 s 95.4% of recurrent fallers compared to 10.8% of single fallers, odds ratio 177.9 CI 95% 39.5-801.2, p<0.001. This was the best predictor of recurrent falls (Table 2) [26].

In a seminal study, Purdon–Martin studied evaluated 130 patients with post- encephalitic Parkinson [27]. He wrote:

In the upright position man stands on a base which is narrow and small relative to his height. A manokin or dummy figure is easily knocked over and man himself is stable only as long as his center of gravity remains within the vertical projection of his base.... Some physical instability is widespread among our patients and the more severely affected are remarkable in that they are unable to preserve their equilibrium not only when they are standing but also when they are sitting.

Purdon- Martin attributed postural instability to a combination of proprioceptive and vestibular dysfunction (sensory symptoms).

Locomotion, the rhythmic movement of the extremities, is generated in the spinal cord [28]. A hierarchy of supra-spinal centers in the cortex and basal ganglia signal the spinal cord. This supra-spinal command network is necessary for initiating walking, turning and stopping. A part of this locomotion network is under dopaminergic control. This motor network is impaired in PD and responds, in part, to dopaminergic therapy [28-31].

The locomotor network interacts with a postural stability network that includes inputs from proprioceptors in the muscles, joints, and tendons as well as inputs from the vestibular nuclei and visual system. This sensory network is not under dopaminergic control [29-34].

Proprioceptive inputs from the lower extremities and their integration into the CNS may, as postulated by Purdon–Martin, be most important in determining postural stability. The inability of recurrent fallers to stand on one leg may be related to an approximately 50% reduction of their proprioceptive input from the ground. Future studies of these phenomena will involve inertial monitoring units and a "fall simulator" to clarify the contribution of impaired body sway, dyskinesias and impaired sensory inputs to falls. Parkinson disease, viewed as a "motor disorder", has a prominent sensory component, one refractory to dopaminergic drugs.

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Table 1: Study 1: Comparison age, PD duration and MDS UPDRS scores fallers vs. non-fallers.

|                      | Non-Fallers | Fallers | p-value |
|----------------------|------------|---------|---------|
| Age                  | 66.9 ± 6.1 | 72.6 ± 5.8 | 0.019   |
| PD Duration          | 5.4 ± 2.2  | 9.3 ± 3.7 | 0.026   |
| MDS-UPDRS Motor Score| 18.9 ± 8.3 | 29.3 ± 10.9 | <0.01   |
| Step Length Meters/Step| 0.6 ± 0.13 | 0.45 ± 0.09 | <0.01   |

Table 2: Study 2: Comparison single versus recurrent fallers.

|                      | Single–Fallers 161 patients | Recurrent Fallers 44 patients | p-value |
|----------------------|-----------------------------|-----------------------------|---------|
| Age (years)          | 67.4 ± 6.7                  | 69.7 ± 9.3                  | NS      |
| PD Duration (years)  | 5.9 ± 4.5                   | 12.6 ± 7.0                  | 0.001 * |
| MDS UPDRS Motor Score| 19.7 ± 8.3                  | 32.3 ± 12.6                 | 0.01*   |
| Step length Meters/Step| 0.52 ± 0.12                | 0.31 ± 0.12                 | <0.01*  |
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