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The relationship between real world ambulatory activity and falls in incident Parkinson's disease: Influence of classification scheme

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ABSTRACT

Introduction: Few studies have categorized falls in early Parkinson's disease (PD) and little is known about falls incidence and evolution. Fall incidence and frequency are reported to be 'U' shaped with respect to disease severity and may be influenced by time spent engaged in ambulatory activity.
Methods: Twelve months prospective falls in an incident PD cohort (n = 111) were reported and the relationship between falls and ambulatory activity was examined in a subgroup (n = 83). Fall events were collected using standardised protocols and were categorized by fall frequency (non-faller, single fall, recurrent falls) and also by a novel classification based on pre-fall event: (1) engaged in advanced activity; (2) ambulation; and (3) transition. Non-parametric statistics compared groups in both classifications.
Results: At baseline 23 (20.7%) of the cohort had fallen, increasing to 41 (36.9%) participants over 12 months. Total time spent walking was significantly lower for transition fallers compared with non-fallers and ambulation fallers ($p = 0.041$), who also had significantly increased disease severity. There were no significant relationships when fallers were categorized by frequency. We present an inverted U curve model depicting the relationship between falls and activity over time in PD, and propose that at this stage transition and ambulation fallers occupy different places on the curve.
Conclusions: Falls are more common than recognised in newly-diagnosed PD. Daily activity is reduced even in early disease for people who fall during transitions. Classification methods that take pre-fall event into account may be useful to understand the heterogeneity of this complex problem.

1. Introduction

Falls affect 35–90% of people with established Parkinson's disease (PD) and between 18 and 65% are recurrent fallers [1]. In addition to the risk of physical injury, falls have a negative psychosocial impact creating a spiral of increased fear of falling and reduced physical activity, and increased likelihood of nursing home admission [2]. Despite presenting such a vast clinical problem, falls predictors are scarce, relying on insensitive markers such as previous falls history [1,3] which has limited clinical utility. This uncertainty is further compounded by the multifactorial aetiology of falling. Poor mobility, visual problems, cognitive impairment, environmental obstacles, freezing of gait, co-morbidities and polypharmacy all influence fall risk [1,3], making interpreting fall causality challenging.

The role of ambulatory activity to the nosology of falls in people with PD is important but there is a paucity of empirical evidence examining this relationship. The inference is that in early disease when falls are relatively infrequent the association between falls and activity is weak, becoming stronger as falls increase whilst ambulatory activity (especially outdoor activity) is maintained. Over time activity tails off and people become more sedentary with a concomitant reduction in falls [3]. This coupling and decoupling can be represented as an inverted U-shaped relationship, possibly mediated by disease severity or secondary consequences of chronic disease. A tension exists between ambulatory activity and risk of falls, in that maintenance of activity is important in postponing or reversing decline in motor abilities associated with PD [4,5] while increased activity levels in people with poor balance responses and/or impulsivity may increase risk of falling. Further work is required

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to understand the nature and evolution of this relationship, which may also be influenced by the frequency [6,7] and context of falls.

Fallers are classified primarily by fall frequency in trials, with recurrent fallers presenting with clinical features contrasting those of single and non-fallers [6, 8]. However this approach does not take fall causality or circumstance into account. Early attempts at classification systems attributed falls to either purely participant-centric or environmental factors [8,9] but recent interest has focused on the importance of the context of falls, in particular the physical action undertaken by the faller immediately prior to falling [10], termed the 'pre-fall event' in this paper. People who fall during positional change such as sit-to-stand or turning are likely to be phenotypically different from those who fall during high-risk activity such as outdoor hiking, as well as being less active.

This study contributes to our understanding of the complex relationship between falls and activity by examining prospective falls in incident PD. The primary aim of this study was to explore the association between 12 month prospective falls and ambulatory activity in our incident cohort of PD. We described fallers using two falls classifications. The first used the established criteria (fall frequency) and the second used novel criteria based on pre-fall event.

2. Methods

2.1. Participants

Participants were recruited into ICICLE-GAIT within 4 months of receiving their PD diagnosis. This is a collaborative study with ICICLE-PD, an incident cohort study (Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation - Parkinson's disease); full description of this cohort is available elsewhere [11]. Briefly, the authors aimed to recruit all incident idiopathic PD cases in Newcastle-upon-Tyne and Gateshead between June 2009 and December 2011. ICICLE-GAIT recruited a subset of the cohort at the same time point. Primary care (general practitioners) and secondary care (neurologists, geriatricians and PD specialist nurses) services were invited to notify the investigators of potential participants. Participants had their PD diagnosis confirmed by a consultant neurologist specialising in neurodegenerative diseases according to the UK Brain Bank Criteria [12]. Exclusion criteria included a diagnosis of parkinsonism prior to study onset and non-idiopathic forms (drug-induced and vascular parkinsonism and atypical parkinsonism syndromes including supranuclear palsy, multiple system atrophy or cortico-basal degeneration). Participants were also excluded if they had significant memory impairment or dementia, as evidenced by a Mini Mental State Examination (MMSE) score <24 or did not have sufficient knowledge of the English language to co-operate with testing. The study was approved by the Newcastle and North Tyneside Research Ethics Committee and all participants gave informed consent.

2.2. Clinical testing

All participants ($n = 121$) underwent a comprehensive clinical assessment on study enrolment. PD severity and motor symptomology were assessed using Hoehn & Yahr (H&Y) and Unified Parkinson's Disease Rating Scale (UPDRS) parts II & III [13]. Motor function and bradykinesia were further assessed using the Timed Chair Stand [14]. Global cognition was assessed using the MMSE [15], depressive symptoms using the Geriatric Depression Scale (GDS) [16], fatigue using the Multidimensional Fatigue Inventory (MFI) [17], and falls and balance efficacy by the Activities Balance Self Confidence Scale (ABC) [18]. Retrospective falls for the previous year based on self-report at interview were recorded.

2.3. Falls diaries

Falls were recorded prospectively using standardised falls diaries [19]. Diaries were sent out on a monthly basis with a pre-paid return envelope. Participants were asked to record if they had fallen in the past month. If yes, they were prompted to provide the date and time of each fall as well as location, preceding activity, perceived cause, position in which they landed and mode of recovery in a structured open-ended statement format. Where participants were unable to complete the diaries personally, due to micrographia or other conditions, their nominated relative or carer took over this role. All reported falls were followed-up with a telephone call from a Senior Research Physiotherapist (DM) to verify information and rectify any missing data. Responses were scrutinised to ensure each reported event met with the accepted definition of falling [20].

2.4. Falls classification

Two systems were used to classify fallers based on the falls diary data over the 12 month period: 'fall frequency' and our novel 'pre-fall event' classification. For the former participants were divided into non-faller, single faller and recurrent faller groups based on the number of prospective falls (0, 1, ≥2 respectively) they had over the 12 month follow-up [6]. Pre-fall event was defined as the activity or action undertaken by the participant immediately prior to falling. Falls were recorded with respect to their pre-fall event and allocated to one of three categories: 1) 'transition,' occurring during changes of posture, e.g. turning, rising from chair; 2) 'ambulation,' everyday walking activities, including stair climbing and 3) 'advanced activity' complex high-risk motor tasks not in-keeping with moderate or severe PD e.g. skiing, hill walking. Initial classification was performed by the author (KM) whilst blinded to other variables in the dataset. Validation of the primary author's classification was undertaken by examination of 20 fall events by three blinded falls researchers (SL, LR, and FJ). The inter-rater reliability of the four researchers was assessed using Fleiss' kappa coefficient and acceptable agreement reached $\kappa = 0.643$ (95% CI 0.513–0.686). Finally each of the fallers in the cohort was placed in one of the three pre-fall event categories depending on their predominant fall type.

2.5. Activity monitoring

Ambulatory activity data was available for 83 participants using the validated activPAL™[1] activity monitor [21]. It is a small (53 × 3 × 7 mm), lightweight (20 g) uniaxial accelerometer-based sensor worn on the upper thigh, with a sampling frequency of 10 Hz which identifies postures such as sitting/lying, standing and walking and the number of steps. Activity is recorded in 15 s windows, and at least one step is required to register the windows as a stepping bout. Participants were fitted with the activPAL™ which was worn for 7 days. Raw data were exported to an Excel[2] spread-sheet for further analysis in MATLAB.[3] The MATLAB program extracted individual ambulatory bouts where a 'bout' was any period of time spent walking. We used four outcomes to describe the volume, pattern and variability of ambulatory activity which are explained elsewhere [22,23]:

1. *Volume:* Proportion of time spent walking per day (summation of all ambulatory bouts, normalised as a percentage of seven days).
2. *Pattern:* [1] Alpha *(α):* defined as the distribution of ambulatory bouts, with a lower α indicating the distribution is derived from a greater proportion of long bouts. α has been described previously in PD research [24] and in healthy older adults [25];
3. *Accumulation of stepping bouts:* Total number of bouts in a period of seven days from which number of steps in each bout were calculated. These variables were combined by summing the total number of steps occurring in bouts of <20 steps, 20–100 steps and >100 steps to give a measure of accumulation of activity.
4. *Variability ($S2_w$):* The 'within subject' variability of bout length. This was calculated from a maximum likelihood technique as the distribution of bout length was log normally distributed [26]. A high $S2_w$ indicates a more varied length of walking bout.

2.6. Data analysis

Data were inspected for normality. In view of non-normal distributions for some variables and the relatively small number of participants in the subgroups we used non-parametric statistics throughout. Demographic, clinical and accelerometry data were described first for the total cohort ($n = 111$) and for both groups of fallers: 1) non-fallers, single and recurrent fallers; and 2) non-fallers, transition and ambulation fallers. Between-group differences were compared using the Kruskal–Wallis test and post-hoc differences were identified using Mann–Whitney U tests. Kaplein–Meyer survival curve analysis was used to assess time to first fall for both faller classifications. Data analysis was conducted using SPSS® 19.0 software.[4]

3. Results

3.1. Participant characteristics

One hundred and twenty one participants were included in the baseline cohort. Ten participants were lost to 12 month follow-up assessment (incomplete falls diaries: 4; withdrew: 3; lost to follow-up: 2 died: 1), leaving a final sample size of 111. At baseline 23 (20.7%) participants reported previous fall(s). Over the 12 month period this increased to 41 (36.9%) participants. Seventy participants did not report any falls. This was a cohort of early PD participants: median PD duration was less than 6 months and >80% of

[1] PAL Technologies, Glasgow, UK.
[2] Microsoft Corp., Redmond, WA, USA.
[3] MathWorks, Natick, MA, USA.
[4] IBM®, Chicago, IL., USA.