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Daytime sleepiness is associated with falls in Parkinson's disease

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Abstract

Falls are frequent in Parkinson's disease (PD), and may be influenced by daytime sleepiness. We reviewed the records of 120 men with PD. Mean Epworth Sleepiness Scale (ESS) values were significantly different between non-fallers and fallers (6.0 vs. 9.7, $p<0.01$). In multivariate analysis, ESS remained significantly associated with falls (OR 1.2, 95% CI 1.1–1.4, p=0.02), along with cognitive impairment (OR 4.4 95% CI 1.0–18.7, p=0.04) and postural instability/gait dysfunction (OR 1.6 95% CI 1.0–2.4, p=0.03) in non-depressed patients. In conclusion, non-depressed PD patients are 20% more likely to fall for every one unit increase in the ESS measure of sleepiness.

Keywords

Parkinson's disease; falls; sleepiness; depression; cognitive impairment

Introduction

Falls are a frequent complication of Parkinson's disease (PD). They occur in more than half of PD patients [1–7]. Falls restrict activities, have a negative impact on quality of life [6,7], and approximately 25–35% of falls result in injury [1,3,7,8]. Prior falls [1,5–7,9], longer disease duration and greater severity [3–7], anxiety and depression [3,5,6], and cognitive impairment [6,9] have all been demonstrated to be risk factors for falls in PD.

In older adults in general, daytime sleepiness as evidenced by napping confers an increased risk of falls, even when adjusting for other risk factors [10,11]. It is thus conceivable that

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The authors have no conflict of interest to report.

excessive daytime sleepiness (EDS) may also contribute to fall risk in PD patients. This is of particular concern because EDS has been demonstrated in 47% of PD patients using objective multiple sleep latency testing [12], and its prevalence exceeds 50% in studies using the Epworth Sleepiness Scale (ESS) for diagnosis [13–15]. However, little is known about the association between EDS and falls in PD.

This study sought to test the hypothesis that PD patients with more severe levels of sleepiness would have increased odds of falling. If present, this association may ultimately provide insights that could lead to new therapeutic options to reduce falls in PD.

Methods

We abstracted data from the electronic health records of new patient visits to the Parkinson's Disease Research, Education and Clinical Center at the Philadelphia Veterans Affairs Medical Center (PVAMC). The study was approved with a waiver of informed consent by the PVAMC IRB.

Inclusion/Exclusion Criteria

Patients seen in the clinic with new visits possibly related to parkinsonism from January 2001 to December 2009 were selected. Charts were reviewed to identify cases of possible PD using established criteria [16].

Variables

Gait—Severity of gait impairment was assessed using the "Postural instability and gait" motor subscale of the Unified Parkinson's Disease Rating Scale (UPDRS) [17]. Since falling is the outcome measure of interest, it was removed from the subscale to create a modified postural instability and gait subscale score.

Falls—Fall history was based on self-report and was determined from the UPDRS fall question ("Falling, unrelated to freezing"). For the data analysis, fall history was dichotomized as either no falls or any history of falls.

Depression—The Geriatric Depression Scale (GDS) short form was used to assess depression symptomatology [18].

Daytime Sleepiness—The Epworth Sleepiness Scale (ESS) is an 8 item instrument that measures daytime sleepiness and has shown acceptable psychometric properties in PD patients [19,20]. Higher values are associated with increased levels of sleepiness [19]. Since there are no established thresholds for identifying excessive sleepiness in PD, the ESS was analyzed as a continuous scale. The ESS was completed by the patient and reviewed by the treating physician.

Cognitive Impairment—Cognitive assessment was performed using three commonly used measures: the Montreal Cognitive Assessment (MoCA)[21], Mini-Mental Status Examination (MMSE) [22] and the St. Louis University Mental Status examination (SLUMS) [23]. Since different cognitive measures were used for different subjects, cognitive status was dichotomized as impaired or not impaired based on the recommended thresholds for each instrument.

Additional data abstracted from the medical record included age, sex, race, years of education, disease duration, Hoehn and Yahr stage, presence or absence of tremor and prior

treatment with PD medications. The clinical record and self-report scales were compared for accuracy and consistency by the abstractor.

Data Analysis

Multivariate models were constructed using logistic regression with presence or absence of falls as the dependent outcome measure. Variables were chosen for inclusion in the model if there was a relationship to falls in bivariate analysis ($p<0.25$) or if considered clinically relevant (age and disease duration). Since depression has a strong relationship to both sleepiness and fall risk and may modify the relationship, a single model testing for this interaction term was created. The interaction between depression and ESS was significant ($p=0.04$). Therefore, the multivariate logistic regression model was stratified by depression status [24,25]. All statistical data analysis was conducted using Stata, version 11 (College Station, TX).

Results

Subject characteristics are presented in Table 1 for all eligible subjects, of whom 82% had ESS and fall data, and 60% had complete data including cognitive status. The characteristics of all eligible subjects, those with ESS/fall data, and those with complete study data are essentially similar. Fifty-two percent reported falls, with 5% falling daily. The ESS was higher in those with a history of falls compared to those with no falls (9.7 +/− 5.3 vs. 6.0 +/− 4.2, respectively, $p<0.01$). Every one unit increase in the ESS was associated with a 20% increased odds of a fall in unadjusted analysis (OR 1.2, 95% CI 1.1–1.3, $p<0.01$). Using a cut-off of 10 on the ESS, fallers were significantly more likely to have excessive daytime sleepiness than non-fallers (40.3% vs. 20.7%, p=0.02). Other factors associated with falls in unadjusted analysis were depression (OR 3.9, 95% CI 1.6–9.4, $p<0.01$), cognitive impairment (OR 2.8, 95% CI 1.3–5.8, $p<0.01$), the modified PIGD (OR 1.6, 95% CI 1.3–2.0, $p<0.01$), Hoehn and Yahr stage greater than 2.5 (OR 3.1, 95% CI 1.5–6.7, $p<0.01$) and prior PD treatment (OR 2.1, 95% CI 1.0–4.4, $p=0.05$). When examining the ESS as a function of depression status, the ESS was markedly higher in patients who met GDS criteria for depression symptoms than in those who did not (10.7 +/− 5.9 vs. 6.8 +/− 4.4, respectively, $p<0.01$). Multivariate models are presented in Table 2. The model that included all subjects (depressed and non-depressed) was statistically significant ($p<0.01$) and explained 23% of the variance in fall risk. The model that included only non-depressed subjects explained 32% of the variance, $p<0.01$. In these non-depressed subjects, the following covariates were significantly associated with an increased risk of falls: modified PIGD, cognitive impairment and ESS. In the analyses that only included subjects with depression, the model was not significant ($p=0.19$).

Discussion

The findings from this retrospective study in male PD patients suggest that daytime sleepiness is significantly associated with falls even when controlling for known fall risk factors such as gait and cognitive status. Among non-depressed PD subjects, for each one point increase in the Epworth Sleepiness Scale (ESS), the odds ratio for a fall was 1.2, which represents a 20% increase in the odds of a fall. The ESS can range from 0 to 24, thus for patients with higher ESS scores and more severe sleepiness, this can translate into a markedly increased risk for falls. These findings suggest that addressing daytime sleepiness may have the potential to reduce falls in PD patients.

These findings contradict the results from a recent small study. Bryant and colleagues studied 54 patients with PD and found that ESS did not differ significantly between fallers and non-fallers (mean ESS 12.17 vs 11.56, respectively) [26]. This study, however, was

limited by a small sample size (n=54), and did not assess for possible confounding or effect modification due to depression or fatigue.

Daytime sleepiness can occur for a variety of reasons in PD patients. Sleep disorders, for example, are especially common in patients with PD. Approximately two-thirds of PD patients suffer from some form of sleep disturbance [27–32]. Additional risk factors for sleep disturbance among PD patients include stiffness, cramps and hallucinations [31,33,34]. Several medications for PD can also cause daytime sleepiness [31,35–37]. Taken together, these conditions can lead to increased rates of EDS [29,38]. EDS could act to increase the risk of falls through a variety of mechanisms such as impaired balance and slower reaction times [39,40].

We did not observe the same relationship between falls and daytime sleepiness in depressed PD patients. This could be related to significant overlap between sleepiness and depression symptoms. Indeed, depressed subjects had significantly higher ESS scores than non-depressed ones in our study. Others have also noted that depression symptoms are associated with sleepiness as identified by the ESS, although this has not been consistently noted in PD [25,41]. Another possibility is that the correlation between subjective and objective sleepiness may be reduced in patients with depression and PD. Alternatively, there may be a threshold effect such that in depressed patients, who have already elevated levels of sleepiness, further increases above a certain levels confer only a small additional increase in fall risk, thus attenuating the association between sleepiness and fall risk.

Our study has several limitations. Most notable is that it is retrospective, and thus cannot establish causal relationships. The reliability of fall recall can also vary [42]. Our data did not include detailed medication information and had inadequate numbers of subjects in each medication category to do additional analyses related to medications. The study cohort consisted of a male cohort receiving their care in the Veterans Affairs system which limits study generalizability. Our study also did not include any objective sleep or daytime sleepiness measures, and analyzed ESS as a continuous variable. It is also important to note that we assessed daytime sleepiness, which is distinct from fatigue in PD patients [43]. The number of subjects with depression was only 35, thus creating a concern for type II error. Furthermore, as evidence by larger confidence intervals for some of the factors (e.g. cognitive impairment), the small sample size will make interpretation of point estimates less reliable. However, the OR for all non-significant associations were fairly small and even with a larger sample size may have remained non-significant. Further studies with larger, more representative cohorts are needed to confirm these preliminary findings.

In this sample, the odds of falling was increased in non-depressed PD patients who experience daytime sleepiness. This effect persisted even after adjusting for other risk factors for falls, including disease duration, gait abnormalities and cognitive impairment. Future research should examine the specific etiologies of sleepiness in PD patients and the effects of their treatment on both daytime sleepiness and falls.

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Table 1

Sample characteristics of cohort of Veterans with Parkinson's disease at initial visit at the Philadelphia VA Medical Center.

	Total Sample (N=199)	Sample with complete ESS and fall data (N=163)	Sample with complete data (N= 120)
Mean age (s.d.)	71.4 (9.7)	71.2 (9.9)	71.4 (9.6)
Male, percent (N)	99.0 (197)	98.8 (161)	100 (120)
Education, years (s.d.)	13.7 (3.2)	13.5 (2.9)	13.5 (3.1)
White race, percent (N)	84.9 (169)	87.1 (142)	87.5 (105)
Non-hispanic. percent (N)	96.0 (191)	96.3 (157)	98.3 (118)
Tremor, percent (N)	86.9 (173)	85.9 (140)	88.3 (106)
GDS score, mean (s.d.)	4.5 (3.9)	4.6 (4.0)	4.4 (3.9)
Depression by GDS, percent (N)	31.5 (52)	32.5 (51)	29.2 (35)
Cognitive impairment, percent (N)	50.0 (82)	54.0 (74)	55.8 (67)
Epworth Sleep Score, mean (s.d.)	8.1 (5.4)	8.1 (5.4)	7.9 (5.1)
Falls, percent (N)	55.2 (107)	57.7 (94)	51.7 (62)
Modified PIGD score, mean (s.d.)	3.5 (2.8)	3.4 (2.7)	3.2 (2.6)
Prior treatment with PD medications, percent (N)	62.3 (124)	63.2 (103)	59.2 (70)

ESS: Epworth Sleepiness Scale. GDS: Geriatric Depression Scale. Modified PIGD: Postural Instability and Gait subscale of the Unified Parkinson's Disease Rating Scale without fall item.

Table 2

Odds ratios from multivariate (adjusted*) analysis of risk factors associated with falls

	Adjusted Odds Ratios (N=120)	Adjusted Odds Ratio for subjects without depression (N=85)	Adjusted Odds Ratio for subjects with depression (N=35)
Age (yr)	1.0 (0.9–1.1, p=0.75)	1.0 (0.9–1.1, p=0.50)	1.0 (0.9–1.1, p=0.37)
Disease duration (mo)	1.0 (0.9–1.1, p=0.83)	1.0 (1.0–1.1, p=0.12)	1.0 (0.9–1.0, p=0.16)
Hoehn and Yahr, stage 2.5 or greater	0.6 (0.2–1.8, p=0.34)	0.4 (0.1–1.8, p=0.21)	1.0 (0.1–4.6, p=0.98)
Cognitive impairment	**2.3 (0.8–6.1, p=0.11)**	**4.4 (1.0–18.7, p=0.04)**	0.4 (0.1–4.1, p=0.41)
ESS, per unit change	**1.1 (1.0–1.2, p=0.05)**	**1.2 (1.0–1.4, p=0.02)**	1.0 (0.8–1.3, p=0.78)
Geriatric Depression Scale (GDS>5)	1.9 (0.6–5.9, p=0.24)	N/A	N/A
Modified PIGD, per unit change	**1.5 (1.1–1.9, p=0.01)**	**1.6 (1.0–2.4, p=0.03)**	**1.7 (1.0–2.9, p=0.05)**
Prior treatment with PD medications	1.4 (0.6–3.5, p=0.49)	1.5 (0.5–5.1, p=0.48)	0.5 (0.1–4.6, p=0.55)

ESS: Epworth Sleepiness Scale. Modified PIGD: Postural Instability and Gait subscale of the Unified Parkinson's Disease Rating Scale with the fall question removed.

*Models adjusted for all other variables listed.