

Depression in veterans with Parkinson's disease: frequency, co-morbidity, and healthcare utilization

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SUMMARY

Objective To determine the frequency of depression in Parkinson's disease (PD) in routine clinical care, and to examine its association with co-morbid psychiatric and medical conditions and healthcare utilization.

Methods Depression diagnoses and healthcare utilization data for all male veterans with PD age 55 or older seen in fiscal year 2002 ($n = 41,162$) were analyzed using Department of Veterans Affairs (VA) national databases. Frequencies of co-morbid disorders and healthcare utilization were determined for depressed and non-depressed patients; associations with depression were examined using multivariate logistic regression models.

Results A depression diagnosis was recorded for 18.5% of PD patients, including major depression in 3.9%. Depression decreased in frequency and severity with increasing age. In multivariate logistic regression models, depressed patients had significantly greater psychiatric and medical co-morbidity, including dementia, psychosis, stroke, congestive heart failure, diabetes, and chronic obstructive pulmonary disease than non-depressed patients (all $p < 0.01$). Depressed PD patients were also significantly more likely to have medical (OR = 1.34, 95% CI = 1.25–1.44) and psychiatric hospitalizations (OR = 2.14, 95% CI = 1.83–2.51), and had more outpatient visits ($p < 0.01$), than non-depressed PD patients in adjusted models.

Conclusion Depression in PD in non-tertiary care settings may not be as common or as severe as that seen in specialty care, though these findings also may reflect under-recognition or diagnostic imprecision. The occurrence of depression in PD is associated with greater psychiatric and medical co-morbidity, and greater healthcare utilization. These findings suggest that screening for depression in PD is important and should be embedded in a comprehensive psychiatric, neuropsychological, and medical evaluation. Copyright © 2006 John Wiley & Sons, Ltd.

KEY WORDS—depression; Parkinson's disease; frequency; co-morbidity; healthcare utilization

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder, after Alzheimer's disease,

affecting approximately one million persons in the United States (Tandberg *et al.*, 1996; de Rijk *et al.*, 1997). Depression is common in PD (Cummings, 1992; Slaughter *et al.*, 2001) and is associated with more rapid decline in activities of daily living (Starkstein *et al.*, 1992), cognitive decline (Marder *et al.*, 1995), reduced quality of life (Kuopio *et al.*, 2000), excess disability (Weintraub *et al.*, 2004), and mortality (Hughes *et al.*, 2004).

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Widely varying rates of depression in PD patients have been reported. Slaughter *et al.* (2001) summarized 44 studies finding that depression rates ranged from 7–70%. Differences in classification, diagnostic tools, demographic characteristics, sample size and severity of PD may contribute to the variation in depression rates. Another important factor is study setting; community-based studies (Hantz *et al.*, 1994; Tandberg *et al.*, 1996; Schrag *et al.*, 2001) have reported lower rates of major depression (3–8%) and depression overall (20–24%) than studies involving patients treated in tertiary care settings. In the latter, rates of major depression ranged from 21–40% and depression overall ranged from 41–54% (Sano *et al.*, 1989; Dooneief *et al.*, 1992; Hoogendijk *et al.*, 1998; Starkstein *et al.*, 1998; Lemke *et al.*, 2005). However, the frequency and types of depression in PD patients receiving routine clinical care are not known.

Regarding co-morbid disorders, both psychosis and cognitive impairment are common in PD (Ismail and Richard, 2004; Aarsland *et al.*, 2005), and studies suggest that there may be increased rates of these symptoms in PD patients with depression (Marder *et al.*, 1995; Kuzis *et al.*, 1997; Marsh *et al.*, 2004). Although an association between depression and many chronic medical conditions in general has been reported (Evans and Charney, 2003), it is not clear if PD patients with depression have excess medical or neurological co-morbidity compared with non-depressed PD patients.

The goals of this study were to report the frequency of depression diagnosed in a large national sample of PD patients receiving routine clinical care, and to examine co-morbid psychiatric and medical conditions and healthcare utilization in this population.

METHODS

Data from fiscal year 2002 were derived from Department of Veterans Affairs (VA) national databases. Subjects with PD were identified using the following codes of International Classification of Diseases 9th Revision, Clinical Modification (ICD9CM, WHO, 1994): idiopathic PD (332.0), other degenerative diseases of the basal ganglia (333.0), and unspecified extrapyramidal disease (333.90). The latter two diagnostic codes were included given diagnostic imprecision that can occur in non-specialty clinics; thus, inclusive rather than exclusive criteria were applied.

As in other studies examining depression in non-psychiatric settings (Unutzer *et al.*, 2002; Valenstein *et al.*, 2004; Alexopoulos *et al.*, 2005), subjects with depression were identified using ICD9CM codes for depressive disorders (296.2x, 296.3x, 296.90, 296.99, 300.4, 311, 293.83, 301.12, 309.0 or 309.1) in order to: (1) capture clinically significant depressive symptoms; (2) acknowledge the diagnostic imprecision commonly seen in primary care settings with regard to depression diagnoses; and (3) account for variability in the clinical presentation of depression in PD (Ehrt *et al.*, 2006).

There were a total of 43,772 subjects with a diagnosis of PD as defined above, the overwhelming majority of whom were male ($n = 43,104$ [98.5%]), and age 55 or above ($n = 41,162$ [94%]). Therefore, only male PD patients age 55 or older (7,599 with depression, 33,563 without depression) were included in our primary analyses. An additional group of male depressed patients age 55 or older without PD ($n = 247,681$) was identified from the same databases and used in our secondary analyses.

Chi-square tests were used to analyze differences for categorical variables and Student's *t*-tests for continuous variables at the 99% significance level (to accommodate for the potential for type I error given the large sample size in this study). Multivariate regression models adjusting for age, marital status and race were used to evaluate possible associations between depression and commonly reported co-morbid conditions (psychosis, dementia, cerebrovascular accidents [CVA], congestive heart failure [CHF], diabetes, and chronic obstructive pulmonary disease [COPD]), and between depression and healthcare utilization. Point estimates (odd ratios) and 95% confidence intervals (95% CIs) were reported. All analyses were performed with SAS statistical software.

RESULTS

Demographic characteristics and frequency of depression

The overall frequency of depression in PD was 18.5%. The frequency of depression decreased with increasing age (Table 1). PD patients with depression were younger, more likely to be Caucasian, and less likely to be married than PD patients without depression.

Types of depression in PD by age group

Major depression accounted for approximately 21.3% of depression cases among PD patients, while

Table 1. Characteristics of patients with Parkinson's disease, male, age 55 or over by depression diagnosis

Characteristic	PD patients with Depression (n = 7,599)	PD patients without Depression (n = 33,563)	p-value
Age group			<0.0001
55–64 (n = 3755)	944 (12.4%)	2811 (8.4%)	
65–74 (n = 14056)	2536 (33.4%)	11520 (34.3%)	
75+ (n = 23351)	4119 (54.2%)	19232 (57.3%)	
Ethnic group			<0.0001
Caucasian (n = 22868)	4825 (63.5%)	18043 (53.8%)	
Non-Caucasian (n = 18294)	2774 (36.5%)	15520 (46.2%)	
Marital status			<0.01
Married (n = 30877)	5583 (73.5%)	25294 (75.4%)	
Not-married (n = 10285)	2016 (26.5%)	8269 (24.6%)	

non-major depressive episodes (labeled as minor depression) accounted for the other 78.7% of cases. The frequency of major depression was higher in patients ages 55–64 (n = 308; 8.2% of entire population age 55–64), than in those 65–74 years old (n = 545; 3.9%; $p < 0.001$), or those age 75 and above (n = 767; 3.3%; $p < 0.001$). The ratio of minor to major depression increased from approximately 2.1 in the 55–64 year-old age group to 3.7 in 65–74 year-old group to 4.4 in those age 75 and above ($p < 0.001$).

Co-morbid disorders in PD by depression diagnosis

Compared with non-depressed PD patients, those with concurrent depression had significantly higher rates of dementia, psychosis, CVA, CHF, diabetes, and COPD (all p -values < 0.01) (Table 2). In the adjusted models, each comorbid condition was significantly associated with presence of depression.

Healthcare utilization in PD by depression diagnosis

Significantly more PD patients with depression had medical and psychiatric hospitalizations over a

12-month period than non-depressed PD patients (Table 3). Results from multivariable logistic regression models (Table 4) showed that depression was independently associated with both psychiatric and medical hospitalizations. In addition, depressed PD patients also had significantly more medical, psychiatric, and total outpatient visits than non-depressed PD patients in both univariate and multivariate analyses.

Secondary analyses

To further investigate whether higher comorbidity was related to depression itself or the combination of PD and depression, we compared the PD patients with depression to a group of older depressed patients without PD. In these analyses, we found that PD patients with depression had a significantly higher frequency of dementia (20.8% vs 5.4%, $p < 0.001$), psychosis (13.9% vs 6.3%, $p < 0.001$), and CVA (14.4% vs 8.6%, $p < 0.001$) compared with depressed patients without PD. There were no significant differences in rates of CHF (10.4% vs 8.9% $p = 0.40$), and depressed patients without PD had significantly higher rates of diabetes (27.4% vs 23.3%, $p < 0.0001$) and COPD (18.1% vs 14.1%, $p < 0.001$) than depressed PD patients.

Table 2. Medical and psychiatric comorbidities by depression diagnosis

Comorbidity	PD patients with depression (n = 7,599)	PD patients without depression (n = 33,563)	p-value	Odds Ratio* (95% Confidence Intervals)
Dementia	1578 (20.8%)	4109 (12.2%)	<0.0001	1.78 (1.67, 1.91)
Psychosis	1059 (13.9%)	3370 (10.0%)	<0.0001	1.11 (1.03, 1.20)
CVA	1095 (14.4%)	3095 (9.2%)	<0.0001	1.42 (1.31, 1.53)
CHF	792 (10.4%)	2582 (7.7%)	<0.0001	1.24 (1.14, 1.35)
Diabetes	1758 (23.3%)	6797 (20.3%)	0.0088	1.09 (1.02, 1.15)
COPD	1072 (14.1%)	3185 (9.5%)	<0.0001	1.36 (1.26, 1.47)

*Logistic regression models of association between depression and each comorbid condition after adjusting for age, race and marital status. CVA = Cerebrovascular accidents; CHF = Congestive heart failure; COPD = Chronic obstructive pulmonary disease.

Table 3. Hospital utilization by depression diagnosis

Type of Care*	PD patients with depression (<i>n</i> = 7599)	PD patients without depression (<i>n</i> = 33,563)	Test statistics
Inpatient admissions			
No. of patients, <i>n</i> (%)	2,165 (28.5%)	5,634 (16.8%)	$X^2 = 552.71, p < 0.0001$
No. of admissions, mean (SD)	2.0 (1.5)	1.8 (1.3)	$t = -6.35, p < 0.0001$
Psychiatric admissions			
No. of patients, <i>n</i> (%)	318 (4.2%)	551 (1.6%)	$X^2 = 193.90, p < 0.0001$
No. of admissions, mean (SD)	1.5 (1.1)	1.5 (1.0)	$t = 0.42, p = 0.6715$
Medical admissions			
No. of patients, <i>n</i> (%)	1,588 (20.9%)	4,293 (12.8%)	$X^2 = 332.51, p < 0.0001$
No. of stays, mean (SD)	1.7 (1.2)	1.6 (1.0)	$t = -4.68, p < 0.0001$
Other institutional care**			
No. of patients, <i>n</i> (%)	915 (12.0%)	2,156 (6.4%)	$X^2 = 283.18, p < 0.0001$
No. of admissions, mean (SD)	1.3 (0.7)	1.2 (0.6)	$t = -3.22, p = 0.0013$
Outpatient care			
No. of patients, <i>n</i> (%)	7,483 (98.5%)	33,024 (98.4%)	$X^2 = 0.25, p = 0.6174$
No. of visits, mean (SD)	27.0 (35.5)	15.9 (22.7)	$t = -25.62, p < 0.0001***$
Psychiatric visits			
No. of patients, <i>n</i> (%)	3,819 (50.2%)	3,878 (11.6%)	$X^2 = 6104.82, p < 0.0001$
No. of visits, mean (SD)	7.6 (22.5)	9.5 (29.9)	$t = 3.17, p < 0.01***$
Medical visits			
No. of patients, <i>n</i> (%)	7,468 (98.3%)	32,995 (98.3%)	$X^2 = 0.037, p = 0.8475$
No. of visits, mean (SD)	23.1 (28.4)	14.8 (18.7)	$t = -24.16, p < 0.0001***$

*Care received over 12-month period in fiscal year of 2002.

**Other institutional inpatient care includes residential rehabilitation, domiciliary and vocational care, and nursing home care.

***All *p*-values < 0.01 after adjusting for age, race, marital status, and comorbid conditions in linear regression models (log-transformed) for association between depression and number of outpatient visits.

As prevalence rates of depression are higher in women in general, and our main study sample included only men, we performed additional analyses to investigate the impact of sex on diagnostic rates. Including male and female patients with PD (*n* = 43,772), rates of depression were higher in women than men in all age groups (age 55 and below: 42.2% vs 30.8%; age 55–64: 41.2% vs 25.0%; age 65–74: 25.3% vs 18.0%; age 75 and older: 22.1% vs 17.6%); however, gender differences diminished with increasing age. As only a small fraction of PD patients in the main study sample were aged 55 and below (4.7%) and aged 55–64 (8.7%), we suspected that the greater gender difference seen in younger-old patients should have less impact on our estimate of overall depression frequency in PD patients. Consistent with this, we found that the weighted (i.e. assuming a population with an equal number of male and female subjects) overall prevalence of depression in PD subjects age 55 or above was 21.7%.

DISCUSSION

We found that depression was common in a national sample of older male veterans with PD, with a diagnosis of depression recorded in approximately

19% of patients. Other findings included a decrease in frequency and severity of depression with increasing age. Depressed compared with non-depressed PD patients had significantly greater psychiatric and medical co-morbidity, including dementia, psychosis, stroke, congestive heart failure, diabetes, and chronic obstructive pulmonary disease. Depressed PD patients were also significantly more likely to have medical and psychiatric hospitalizations, and had more outpatient visits than non-depressed PD patients.

Most depression cases were recorded as episodes of non-major depression. While this may represent diagnostic non-specificity in non-psychiatric settings, these findings are consistent with recent epidemiological literature that minor forms of depression are far more common than major depression in PD. A community-based study of 245 subjects with PD revealed major depression in 7.7% and minor depression in 45.3% of patients (Tandberg *et al.*, 1996). A multi-site study of 657 PD patients found minor depression was twice as common as moderate to severe depression, as measured with a depression rating scale (Lemke *et al.*, 2005). Overall, it is estimated that major depression may occur in 5–10% of PD patients, with an additional 10–30% experiencing depression of milder severity (Weintraub, 2004).

Table 4. Predictors of hospitalization for Parkinson's disease patients*

Independent variables	Odds Ratio (95% CI)	<i>p</i>
Model 1: all cause of hospitalization		
Depression	1.50 (1.40–1.60)	<0.0001
Psychosis	2.99 (2.88–3.36)	<0.0001
Dementia	4.19 (3.91–4.50)	<0.0001
CVA	2.97 (2.75–3.22)	<0.0001
CHF	3.11 (2.85–3.39)	<0.0001
Diabetes	1.49 (1.40–1.60)	<0.0001
COPD	2.61 (2.41–2.82)	<0.0001
Model 2: medical hospitalization		
Depression	1.34 (1.25–1.44)	<0.0001
Psychosis	1.75 (1.61–1.90)	<0.0001
Dementia	2.87 (2.66–3.09)	<0.0001
CVA	2.76 (2.54–2.99)	<0.0001
CHF	3.38 (3.10–3.69)	<0.0001
Diabetes	1.63 (1.52–1.74)	<0.0001
COPD	2.61 (2.41–2.83)	<0.0001
Model 3: psychiatric hospitalization		
Depression	2.14 (1.83–2.51)	<0.0001
Psychosis	18.53 (15.64–21.95)	<0.0001
Dementia	3.06 (2.59–3.61)	<0.0001
CVA	1.37 (1.12–1.67)	0.0018
CHF	0.86 (1.67–1.12)	0.2631
Diabetes	1.18 (0.997–1.40)	0.0543
COPD	1.65 (1.37–1.98)	<0.0001

CVA = Cerebrovascular accidents; CHF = Congestive heart failure; COPD = Chronic obstructive pulmonary disease.

*Multivariate logistic regression models adjusted for age, race, marital status.

We also found that with increasing age, major depression significantly decreased and minor depression increased. These findings are consistent with those from the general population (Katz *et al.*, 2005), and may reflect possible attenuation in depression severity with increasing age, both in general and in PD patients.

Other findings included the association between depression in PD and greater psychiatric and medical co-morbidity. In secondary analyses comparing patients with PD and depression to depressed patients without PD, we found that while the combination of PD and depression was significantly associated with certain comorbidities (dementia, psychosis, and CVA), it was not associated with others (CHF, diabetes, COPD). The findings support the well-reported association between depression and both psychiatric and medical comorbidity (Geerlings *et al.*, 2000), with possible PD-specific additive or protective effects.

While it is not surprising that psychosis, dementia and depression were major predictors of psychiatric

hospitalizations, and CHF, CVA, COPD, and dementia were major predictors of medical hospitalizations, our findings demonstrate that depression is an independent predictor of both psychiatric and medical hospitalizations in PD. Depression, either through biological or psychological mechanisms, may lead to greater severity of medical co-morbidity and/or to increased healthcare-seeking behavior.

Our results should be interpreted with caution, given that all patients studied were male veterans age 55 or older. This may have led to an underestimation of the overall prevalence rate of depression in PD, so the findings cannot be generalized to nonveterans, females, or younger PD patients. It is also possible that depression was under-recognized in our sample of patients receiving routine clinical care. If so, it may have resulted in part from: (1) diagnosis-related issues such as symptom overlap between PD and depression; (2) atypical features of depression in some patients (Ehrt *et al.*, 2006); (3) patient-related issues such as poor recognition or reporting of symptoms; or (4) delivery of care-related factors such as limited time to assess depression or low rates of depression screening in primary care and neurology clinics (Shulman *et al.*, 2002; Weintraub *et al.*, 2003). However, the relatively lower frequency of depression found in our study is consistent with recent research that depression in PD is not as common in patients seen in non-tertiary care settings (Tandberg *et al.*, 1996). Other limitations include the retrospective nature of study and the use of administrative databases, which did not allow us to assess the accuracy of psychiatric, neurological, or medical diagnoses.

In conclusion, these findings suggest that depression in PD is common in routine clinical care settings, though not as common or as severe as seen in tertiary care settings, and is associated with both greater psychiatric and medical co-morbidity and with increased healthcare utilization. They highlight the importance of screening for depression and co-morbidities in this population. They also provide further evidence in support of recently published clinical guidelines developed by the American Academy of Neurology and quality of care indicators developed by the VA Parkinson's Disease Research, Education, and Clinical Centers (PADRECC's) that endorse a comprehensive psychiatric, neuropsychological, and medical evaluation (Cheng *et al.*, 2004; Miyasaki *et al.*, 2006). In addition, future health services studies should address ways to better coordinate care for PD patients that is delivered in mental health, primary care, and neurology settings.

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