An Estimate of the Prevalence of Dementia in Idiopathic Parkinson's Disease

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A review of the records for evidence of dementia using criteria adapted from the third edition of the Diagnostic and Statistical Manual of Mental Disorders in every patient (hospitalized and outpatient) with parkinsonism at a major medical center during an 18-month period revealed an overall prevalence of 10.9% in 339 patients with idiopathic Parkinson's disease. Demented patients were older, had a later age at onset of motor manifestations, and a more rapid progression of physical disability than nondemented patients. Duration of illness and levodopa use and the presence of tremor or depression were similar in demented and nondemented patients. Demented patients more often responded poorly or developed adverse effects to levodopa than nondemented patients. When Parkinson's disease began after age 70 years, dementia was noted over three times more frequently than when the disease began at an earlier age. The age-specific prevalence rate of dementia for patients older than 70 years was more than twice that for younger patients. Moreover, the number of records with evidence for dementia with idiopathic Parkinson's disease was 3.75 times greater than expected in comparison with data from a study of the prevalence of dementia in the elderly.

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The prevalence of dementia in Parkinson's disease (PD) is unsettled; estimates range from 14% to 40%.1 Brown and Marsden2 reviewed 17 studies reported over the last 60 years that included a total of 2530 patients with PD. Thirty-five percent of these patients had some degree of dementia, but the prevalence of dementia could have been overestimated because of sampling variability and differences in criteria used for the diagnosis of dementia or idiopathic PD.

To estimate the frequency of dementia in PD, we reviewed the records of over 422 patients with parkinsonism from an urban hospital population, using standardized research criteria for dementia and idiopathic PD. Of the records with sufficient evidence to warrant a diagnosis of dementia, 10.9% of the 339 patients with idiopathic PD were demented. Compared with a data set from a standard population of elderly adults older than 60 years, the odds of developing dementia appear to be almost four times greater for patients with idiopathic PD.3

SUBJECTS AND METHODS

We reviewed the records of every patient (hospitalized or outpatient) with parkinsonism in a major teaching hospital seen on all services during the 18 months between March 1, 1983, and Sept 30, 1984. The population included both private and clinic patients. Although the hospital is a tertiary care institution, 90% of the patients came from the greater New York area and were followed up annually. The population was representative of a large urban hospital-based cohort. When a patient had more than one visit (hospital and/or outpatient visits) during the study period, only the first encounter was used in estimating the prevalence of dementia. All available information, including that from subsequent chart entries, was used to substantiate a diagnosis regardless of when it was recorded, however.

Data Extraction

A systematic data collection form to extract clinical information from records was designed by us before the survey. Consensus on criteria for the diagnoses to be described below was reached before the study, and the data form was used in a brief pilot survey before the final data extraction began.

Diagnoses

Criteria for the diagnosis of idiopathic PD included the presence of at least two of the four characteristic motor manifestations of the disorder (tremor, shuffling gait, bradykinesia, or muscular rigidity) with a history of insidious onset. Patients with parkinsonism, resulting from encephalitis, medications, or multiple stroke, were eliminated from further consideration, as were patients with progressive supranuclear palsy.

We based our research diagnostic criteria for primary degenerative dementia and major depression on the definitions in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III).4 Briefly, we considered insufficient criteria for this diagnosis. In some patients quantitative neuropsychological data were present, allowing a more precise diagnosis. The diagnosis of dementia or idiopathic PD was retracted only if it was later refuted, in the record, by a qualified physician, such as a neurologist or psychiatrist. This is similar to the method used by Rajput et al.5 We defined depression as a dysphoric mood characterized by feelings of sadness and associated with changes in appetite and sleep habits.

We also recorded other features of PD: age at onset (defined as the time that the diagnosis of PD was first made by a qualified physician) and duration of PD motor manifestations (defined as the period from the onset of the illness to the first encounter recorded during the study period). In almost half of the patients, disease severity, including the presence of dementia or depression, had been rated on the Columbia University PD rating scale.6 Ability to perform activities of daily living (ADL) was also usually rated.7 The disease was classified as tremulous or nontremulous type, depending on the presence or absence of a resting tremor. Response to levodopa therapy was ascertained: patients were classified as responders (good response to average dosages), secondary nonresponders (ie, good response at first but later not adequate despite sufficient

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Interrater agreement, which we reviewed, was 3.95, which is chance corrected. 

Comparison Group

Because we wanted to estimate the frequency of dementia expected at this age, we used prevalence data from the Baltimore Longitudinal Study (BLS) for comparison. That study included volunteers older than the age of 60 years. By multiplying the number of patients with PD in each age group by the age-specific prevalence rate observed in the BLS we could estimate the number of cases of dementia that might have been expected in people older than the age of 70 years.

RESULTS

The records of 422 patients with parkinsonism were reviewed; of these, 355 were judged to have idiopathic PD. Sixteen of the patients with idiopathic PD had the onset of motor symptoms before the age of 40 years and were excluded from further analysis because of the unusual age of onset. This left 339 patients in the study: 264 (78%) were outpatients and 75 (22%) were hospitalized during the study period. A mental status examination was not recorded in three patients, but their data were still included in the study without a diagnosis regarding dementia to maintain a conservative prevalence estimate.

Of the 75 hospitalized patients, 50 were admitted for various problems related to PD, such as medication adjustments or drug trials. Another 25 were hospitalized for medical or surgical problems unrelated to PD, such as myocardial infarction or pneumonia.

We found sufficient evidence for dementia in the records of 37 (10.9%) of the 339 study patients with PD seen during the prevalence period. Dementia was recorded in the charts of 18 (24%) of 75 hospitalized patients and 19 (7%) of 264 outpatients (z = 3.95, P < .001). Demented patients were significantly older (74.03 ± 8.17 years vs 66.91 ± 9.92 years; P < .01), had a later age at onset of the motor manifestations of PD (65.28 ± 10.43 years vs 59.25 ± 9.67 years; P < .01), had more severe manifestations (measured by the Columbia University PD rating scale: 50.32 ± 19.27 vs 31.46 ± 18.12, P < .01), and were significantly more disabled than the patients without dementia (measured by the Schwab and England ADL scale: 44.0% ± 21.97% vs 74.55% ± 20.39%, P < .01). The proportion of demented patients whose motor manifestations began after the age of 70 years was significantly greater than the proportion of demented patients whose motor manifestations began at an earlier age (<69 years, 23 [8.5%] of 272, >70 years, 14 [20.9%] of 67: z = 2.933, P < .001). Demented patients more often had a rapid progression of disability than the nondemented patients (14.4% P < .05). Development of illness, levodopa use and mean dosage, type of PD (tremulous vs non tremulous), and prevalence of depression (47% in the total sample) were similar in demented and nondemented patients. However, the frequency of demented patients classified as either primary or secondary nonresponders to dopaminergic medications and the number developing adverse effects at relatively low doses was significantly greater than in the nondemented group (x² = 9.41, P < .01). Onset of PD (motor manifestations) after age 70 years occurred more often in the demented than in the nondemented patients (x² = 11.41, P < .01); the prevalence odds ratio for dementia in patients with onset of PD after the age of 70 years compared with those with onset before the age of 70 years was 3.75 (95% confidence interval, 1.75, 7.95).

Thirty-seven patients had taken the Modified Mini-Mental State Examination at the time of their entry into the prevalence survey. Although the number of patients tested was small, the results agreed with the chart reviews. There were 33 nondemented patients (mean score, 51.0) and four demented patients (mean score, 24.5) (z = 4.33, P < .02). The total score for the Modified Mini-Mental State Examination is 57, and mean for elderly control subjects is 52.3 ± 17.

No differences were apparent in the prevalence of dementia, age of onset, or duration of illness when the information was collected near the time of an office visit or extracted at a later date from the record. Interrater agreement for the diagnosis of dementia from the medical records was 91% between the three independent reviewers. After correcting for chance agreement, the x² statistic indicated that the agreement between the reviewers was 88%. The agreement between these reviewers and the originally collected data was also high: 87%.

To compare the prevalence of dementia in our study with a standard population we used the data from the BLS. We compared the prevalence of dementia in the 272 patients older than 60 years with idiopathic PD from our study with that data set; dementia was found 3.84 times more often than expected for that age group (Table). When PD began before the age of 70 years, dementia was noted in the records 4.8 times more often than would have been expected based on the BLS data, but when PD began after the age of 70 years, dementia was recorded 2.73 times more often than expected.

COMMENT

Using standardized criteria for dementia and for idiopathic PD, we found evidence of dementia in the records of 10.9% of patients with PD. While this may support the claim that the overall prevalence of dementia in Parkinson's Disease—Mayeux et al

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Prevalence of Dementia in Parkinson's Disease (PD) Compared With Baltimore Longitudinal Study Sample

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Observed</th>
<th>Expected</th>
<th>SMR*</th>
<th>95% CI (SMR)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients with PD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>older than 60 y</td>
<td>272</td>
<td>36</td>
<td>9.98</td>
<td>3.84</td>
<td>(2.69, 5.19)</td>
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<tr>
<td>PD onset before 70 y</td>
<td>221</td>
<td>23</td>
<td>4.79</td>
<td>4.80</td>
<td>(3.04, 6.90)</td>
</tr>
<tr>
<td>PD onset after 70 y</td>
<td>51</td>
<td>13</td>
<td>4.75</td>
<td>2.73</td>
<td>(1.45, 4.43)</td>
</tr>
</tbody>
</table>

*SMR indicates standardized morbidity ratio.
†95% CI (SMR) indicates 95% confidence interval for the SMR.
PD has been overestimated,\textsuperscript{2,10} it must be realized that we also found age-specific prevalence rates to increase after age 60 years. The retrospective and cross-sectional nature of the chart review makes it likely that we identified only severe dementia and underestimated the prevalence of mild dementia. We also may have slightly underestimated dementia by determining rates based on the first encounter during the prevalence period. However, our results do indicate that dementia in patients with PD is almost four times more frequent than expected in people older than the age of 60 years.

Although the prevalence of dementia in the general population increases with advanced age, the standardized morbidity ratios indicate that the prevalence of dementia in this cohort with idiopathic PD is almost five times that expected for healthy people younger than the age of 70 years and almost three times greater than expected for healthy people older than 70 years. The reduction in the standardized morbidity ratio after the age of 70 years probably reflects the increased prevalence of dementia in the general population at that age. The comparison of our data to the BLS\textsuperscript{3} is only speculative because of major methodologic differences. Nevertheless, it implies that patients with idiopathic PD are at greater risk for dementia than is the general population regardless of when the motor manifestations begin.

In this study we found demented patients with PD to be older than non-demented patients and to have a more rapid progression of illness and greater disability, as others have found.\textsuperscript{11,13} Although duration of PD is similar in demented and non-demented patients, the onset of dementia may reduce survival. Mindham et al.\textsuperscript{14} reported that four of 16 demented patients died within three years, compared with two of the 24 nondemented patients.

Estimates of the prevalence of intellectual decline, including dementia, in PD vary considerably.\textsuperscript{1 Brown and Marsden\textsuperscript{2} consider this variation to be due to differences in methods, such as the use of nonstandardized criteria for dementia and PD. Three separate studies of dementia in PD\textsuperscript{11,13} used similar mental status assessments. Adjusting the prevalence rates to satisfy DSM-III criteria for dementia indicates that about 15% of the almost 1000 patients in these three studies were demented. This still suggests that the prevalence of dementia is greater than in control subjects, and Lees\textsuperscript{4} and Taylor et al.\textsuperscript{15} support this amended prevalence data. In one Northampton region of the United Kingdom, the prevalence of idiopathic PD was 108.4 per 100,000, and 11% of the 223 patients with idiopathic PD were demented by a reasonable assessment of mental function and disability although there were no control subjects.\textsuperscript{16} However, in our study we found the age-specific rates of dementia in PD to increase significantly after the age of 70 years, as did Marttila and Rinne.\textsuperscript{17}

Rajput et al.\textsuperscript{18} found that the probability of developing dementia was greater in patients with idiopathic PD than in a comparison group of similarly aged adults. The cumulative probability of dementia was 21.1% for patients with PD compared with 5.7% for control subjects after five years.

Because there is a remarkable overlap in the clinical,\textsuperscript{16,17} biochemical,\textsuperscript{19} and pathological\textsuperscript{18,20} manifestations of dementia in PD and in Alzheimer's disease, the cause of dementia in PD is of interest. Idiopathic PD may predispose to dementia. However, the only known risk factor is a late age at disease onset. In addition, some types of intellectual impairment in PD do not warrant a diagnosis of dementia,\textsuperscript{12,21} and postmortem studies are often inconclusive.

Using DSM-III criteria, it is apparent that most patients with idiopathic PD are not demented. Our data must be interpreted with caution because we may have identified only severe dementia, they were collected retrospectively, and we used an external comparison group. Nevertheless, our results suggest that while the prevalence of dementia is relatively low, the odds of becoming demented with idiopathic PD, compared with a standard population, may be significantly increased.

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\textbf{References}


