Prevalence and Clinical Correlates of Psychotic Symptoms in Parkinson Disease

A Community-Based Study

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Background: Hallucinations and delusions are frequent in patients with Parkinson disease (PD) and may have severe clinical consequences for those patients and their caregivers. However, the prevalence and clinical features of these symptoms have not been studied in a representative sample.

Objective: To study the prevalence and clinical correlates of psychosis in a population-based sample of patients with PD.

Method: Total ascertainment of patients with PD in a defined geographical area in Norway was attempted through a detailed community study. Clinical evaluation consisted of a neurologic examination and assessments of depression and cognition. Psychosis was assessed with the thought disorder subscale of the Unified Parkinson's Disease Rating Scale.

Results: A total of 245 patients with PD were identified, 235 (95.9%) of whom participated in this study. Twenty-three patients (9.8%) had hallucinations with insight retained, and another 14 patients (6.0%) had more severe hallucinations or delusions. Psychotic symptoms were associated with age, stage and diagnostic subgroup of PD, severity of depression, and cognitive impairment. Type, duration, and dose of antiparkinson drug therapy did not differ between those patients with PD who had or did not have psychosis. In a polychotomous logistic regression analysis, severity of depression, cognitive impairment, and impairment of activities of daily living were the only significant concomitants of psychosis.

Conclusions: Hallucinations and delusions are common in patients with PD. More advanced and widespread brain changes seem to increase the risk for developing psychosis in patients with PD receiving levodopa therapy.

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In patients with Parkinson disease (PD), neuropsychiatric symptoms frequently accompany motor manifestations of the disease. Psychotic symptoms, ie, disturbances of perception and thought, are among the most frequent and troublesome of these behavioral disturbances. Hallucinations, usually of visual modality, occur in about 30% of patients with PD, and delusions have been found in 10%. In a recent study, visual hallucinations were reported in 26% of patients with PD. The exact frequency of such symptoms has not been established because most previous studies included only small and selected samples of patients and used different definitions of PD and psychiatric disorders.

Hallucinations and delusions in patients with PD were reported before the introduction of dopaminergic therapy but are usually considered to represent behavioral complications of drug treatment, possibly mediated through hypersensitive dopaminergic receptors in the limbic cortex. Some evidence suggests that dementia, advanced age, administration of high daily doses of levodopa, premorbid psychiatric illness, and multidrug therapy are risk factors for psychotic symptoms in PD, but again, systematic studies with large representative samples are lacking.

Psychotic symptoms pose considerable stress on patients and caregivers and have been suggested to increase the risk of nursing home placement and death in patients with advanced PD. Results of recent open-label studies indicate that clozapine administration is effective in treating these phenomena. Thus, psychosis is a common and potentially treatable condition in patients with PD, with severe clinical consequences for patients and caregivers. Knowledge of these phenomena and their association with other clinical characteristics of PD is important for the diagnosis and treatment of patients and can provide information...
PATIENTS AND METHODS

STUDY POPULATION AND CASE ASCERTAINMENT

The study population comprised all patients living in 9 municipalities in the southern part of Rogaland county, Western Norway. The Norwegian Public Health Care System is closely monitored and well developed and organized. All patients with PD must see a specialist in neurology to receive their first prescription of levodopa. Most patients with recognized PD in the study area were treated and monitored by staff members of the Department of Neurology at Rogaland Central Hospital, Stavanger, Norway, and only a few patients were, for special reasons, the responsibility of a general practitioner alone. This is the only department of neurology in the area, and there are no neurologists in private practice outside the hospital.

Total ascertainment of patients with recognized idiopathic PD in this defined geographical area was attempted. The main source of patient information was the medical records of the outpatient clinic of the Department of Neurology. Additional sources were the main patient records of Rogaland Central Hospital. These patient records included information about the diagnosis of every inpatient referred to the hospital since 1972. Furthermore, all general practitioners, nursing home managers, and physicians in charge of nursing homes, district nurses, and home health care workers in the study area were contacted in writing and asked for information about patients with symptoms of Parkinsonism. Information about all members of the local branch of the PD society was also available.

All nursing home physicians and managers, district nurses, and home health workers and 75% of general practitioners responded to the written inquiry. Based on these sources, nearly 500 patients were considered for diagnostic evaluation. Based on information from the hospital records, some patients were excluded because of not having PD. Nearly 400 patients were invited to participate, interviewed, and examined between September 1992 and May 1993 by a neurologist in the study group (J.P.L.). Prevalence rate in the study area on January 1, 1993, was calculated.8

RESULTS

PREVALENCE OF PSYCHOTIC SYMPTOMS

A total of 245 patients with PD were identified, yielding a crude prevalence rate of 110.9 per 100,000 inhabitants. This finding is similar to that of other epidemiological studies of PD. The population with PD included 120 men and 125 women (mean age, 73.6 ± 8.5 years). Mean duration of PD was 9.1 ± 5.8 years. Further details regarding patient selection and demographic data have been published elsewhere.8

Data on the UPDRS thought disorder subscale scores were available for 238 of 245 patients with PD. Three patients died before the examination program was completed; 2 patients had severe end-stage dementia that made clinical evaluation impossible; and 2 patients refused to participate. Three patients received neuroleptic treatment for a psychotic disorder before the diagnosis of PD and were therefore excluded. Thus, 235 (95.9%) of 245 patients were included in this study. Sixty patients (25.5%) experienced vivid dreams (a score of 1 on the UPDRS thought disorder subscale), 23 patients (9.8%) had hallucinations with insight retained (thought disorder subscale score of 2), and 14 patients (6.0%) had psychosis with hallucinations or delusions (thought disorder subscale score of 3 or 4) during the week before evaluation. Among the 48 patients who lived in a nursing home or a home for the elderly, 22.9% reported hallucinations with insight and 18.8% had psychosis. The percentages of patients reporting to have experienced vivid dreams, hallucinations with insight, and psychosis at some point after diagnosis of PD were 26.8%, 11.5%, and 13.6%, respectively.

DIAGNOSIS AND CLINICAL EVALUATION OF PD

All patients were interviewed and examined in an evaluation program consisting of 2 consecutive 1-hour consultations held within 1 month. A semistructured interview was performed to obtain information about disease history, drug therapy, response to levodopa administration, and demographic variables. The clinical examination of motor symptoms consisted of a complete Unified Parkinson’s Disease Rating Scale (UPDRS) assessment, including the Hoehn and Yahr scale.10 Diagnostic evaluation was based on clinical information obtained at the primary evaluation, including disease development and response to levodopa therapy. To achieve high diagnostic accuracy without sacrificing sensitivity, a new diagnostic classification defining clinically definite, probable, and possible PD was used.11 Other neurologic diagnoses or current or previous use of neuroleptic drugs would have excluded a diagnosis of PD in this study.

DIAGNOSTIC GROUPS

Definite Clinical Idiopathic PD

A definite diagnosis required that a patient have resting tremor and at least 2 more cardinal signs: (1) akinesia or bradykinesia, (2) rigidity, or (3) postural abnormalities. The disease has unilateral onset and development, and response to administration of a dopaminergic agent is good to excellent. No clinically significant changes on computed tomographic or magnetic resonance imaging scans should be present.

Probable Clinical Idiopathic PD

For a diagnosis of probable PD, the patient must have fulfilled at least 2 of the 4 clinical criteria from the definite PD category. Resting tremor was not mandatory, and a maximum of 1 of the following atypical clinical features may be present: (1) mild dementia or clinically relevant autonomic failure at disease onset, (2) symmetrical disease presentation, or (3) moderate response to administration of a dopaminergic agent.
Possible Clinical Idiopathic PD

For a diagnosis of possible PD, the patient must have had at least 2 of the 4 cardinal signs. The response to use of a dopaminergic agent should be at least moderate. Mild-to-moderate dementia and autonomic failure at disease onset was allowed.

NEUROPSYCHIATRIC ASSESSMENT

Assessment of Cognitive Functioning

A neurologist conducted a semistructured interview with the patient and caregiver with detailed knowledge of the patient. The Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R), criteria for dementia was used, taking into account the physical disability in PD. Cognitive functioning was rated using the Mini–Mental State Examination (MMSE); the intellectual impairment subscale of UPDRS, which rates intellectual impairment (memory, orientation, problem solving, function at home, and personal care); and the Gottfries, Brâne, and Steen scale. This scale is divided into 4 subscales that estimate motor, intellectual, and emotional, and other symptoms characteristic of dementia. To qualify for a diagnosis of dementia, the patients had to meet the DSM-III-R criteria for dementia at the interview. In addition, at least 1 of the following criteria had to be fulfilled: (1) an MMSE score of less than 24; (2) impairment on at least 3 items of the intellectual subscale of the Gottfries, Brâne, and Steen scale, other than the items “wakefulness” and “ability to increase tempo”; or (3) a score of 2 or more on UPDRS item 1 (intellectual impairment) on subscale 1. Further details of the cognitive assessment are presented elsewhere. 

Assessment of Depression

Depressive symptoms were assessed with a semistructured interview of the patient and caregiver using the DSM-III-R criteria for major depression. The severity of depressive symptoms was scored using the Montgomery and Åsberg Depression Rating Scale (MADRS).

Assessment of Psychotic Symptoms

The presence of hallucinations and delusions during the week before evaluation was assessed using the UPDRS thought disorder subscale, based on a clinical interview with the patient and caregiver. On this scale, no symptoms is scored as 0; vivid dreamings, 1; hallucinations with retained insight (“benign hallucinations”), 2; occasional to frequent hallucinations or delusions without insight that could interfere with daily activities, 3; and persistent hallucinations, delusions, or florid psychosis with lost ability to care for self, 4. Disturbances of perception and thought were thus seen as a continuum, ranging from vivid dreams via hallucinations to delusions with disturbed behavior. A score of 3 or 4 was defined as psychosis. Patients and caregivers were also asked if hallucinations or delusions had ever been present after diagnosis of PD, and severity was scored according to the UPDRS thought disorder subscale.

PROCEDURE AND STATISTICAL ANALYSIS

Data analysis consisted primarily of calculating rates and proportions. To test whether patients with different thought disorder subscale scores differed on demographic and clinical variables, comparisons of continuous data were carried out using 1-way analysis of variance. The Scheffe multiple comparison procedure was used to determine which group means were different from each other. Categorical data (levodopa dosage, sex, presence of dementia or major depression, Hoehn and Yahr stage, and diagnostic subgroup of PD) were analyzed using the linear-by-linear association test. A nonparametric method (Kruskal-Wallis test) was used to test whether thought disorder subscale scores differed among patients with different antiparkinsonian drug regimens and levodopa doses. Polychotomous logistic regression analysis (program BMDP PR) used in a nonstepwise manner was performed to identify predictors of psychosis. Data are presented as mean ± SD.
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Table 1. Clinical and Demographic Characteristics of Parkinsonian Patients With Hallucinations and Psychosis*  

<table>
<thead>
<tr>
<th>UPDRS Thought Disorder Subscale Score</th>
<th>No Disorder (n = 138)</th>
<th>Vivid Dreams (n = 60)</th>
<th>Hallucinations With Insight (n = 23)</th>
<th>Psychosis (n = 14)</th>
<th>Total Group (N = 235)</th>
<th>Statistic†</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>72.5 ± 9.2</td>
<td>73.0 ± 6.7</td>
<td>78.8 ± 6.5</td>
<td>77.1 ± 7.1</td>
<td>73.5 ± 8.5</td>
<td>4.9</td>
<td>.003</td>
</tr>
<tr>
<td>Age at onset of PD, y</td>
<td>63.7 ± 10.4</td>
<td>64.2 ± 9.2</td>
<td>68.5 ± 9.2</td>
<td>65.0 ± 8.3</td>
<td>64.9 ± 9.9</td>
<td>1.6</td>
<td>.20</td>
</tr>
<tr>
<td>Duration of PD, y</td>
<td>8.8 ± 5.7</td>
<td>8.8 ± 5.2</td>
<td>10.3 ± 5.4</td>
<td>12.1 ± 9.0</td>
<td>9.1 ± 5.8</td>
<td>1.9</td>
<td>.13</td>
</tr>
<tr>
<td>Duration of treatment, y</td>
<td>5.9 ± 5.1</td>
<td>6.4 ± 4.9</td>
<td>7.7 ± 4.7</td>
<td>9.1 ± 8.2</td>
<td>6.4 ± 5.3</td>
<td>7.1†</td>
<td>.07</td>
</tr>
<tr>
<td>Levodopa dose, mg</td>
<td>463 ± 203</td>
<td>579 ± 297</td>
<td>509 ± 206</td>
<td>507 ± 262</td>
<td>500 ± 238</td>
<td>7.3‡</td>
<td>.06</td>
</tr>
<tr>
<td>MADRS score</td>
<td>6.6 ± 5.8</td>
<td>8.6 ± 5.4</td>
<td>12.0 ± 4.9</td>
<td>16.0 ± 9.1</td>
<td>8.1 ± 6.3</td>
<td>14.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MMSE score</td>
<td>26.0 ± 5.5</td>
<td>26.2 ± 3.6</td>
<td>18.1 ± 8.5</td>
<td>13.5 ± 9.4</td>
<td>24.5 ± 6.8</td>
<td>31.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>UPDRS ADL score</td>
<td>12.4 ± 7.6</td>
<td>14.1 ± 7.2</td>
<td>22.8 ± 9.9</td>
<td>25.9 ± 10.1</td>
<td>14.7 ± 9.0</td>
<td>22.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>UPDRS motor score</td>
<td>24.0 ± 13.4</td>
<td>27.6 ± 13.5</td>
<td>44.7 ± 15.4</td>
<td>46.1 ± 18.6</td>
<td>28.2 ± 15.8</td>
<td>22.5</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Values are given as mean ± SD. UPDRS indicates Unified Parkinson’s Disease Rating Scale; PD, Parkinson disease; MADRS, Montgomery and Åsberg Depression Rating Scale; MMSE, Mini–Mental State Examination; and UPDRS ADL and UPDRS motor, the activities of daily living and motor subscales of the UPDRS.
† F value (1-way analysis of variance). See text for individual group comparisons using the Scheffé multiple comparison procedure.
‡ χ² (Kruskal-Wallis test).

Table 2. Distribution of Sex, Dementia, Major Depression, and Diagnostic Subgroups Among Parkinsonian Patients With Different UPDRS Thought Disorder Subscale Scores*  

<table>
<thead>
<tr>
<th>UPDRS Thought Disorder Subscale Score</th>
<th>No Disorder (n = 138)</th>
<th>Vivid Dreams (n = 60)</th>
<th>Hallucinations With Insight (n = 23)</th>
<th>Psychosis (n = 14)</th>
<th>Total Group (N = 235)</th>
<th>LL</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>71 (51.4)</td>
<td>31 (51.7)</td>
<td>11 (47.8)</td>
<td>6 (42.9)</td>
<td>119 (50.6)</td>
<td>0.3</td>
<td>.56</td>
</tr>
<tr>
<td>Dementia</td>
<td>27 (19.6)</td>
<td>12 (20.0)</td>
<td>14 (60.9)</td>
<td>11 (78.6)</td>
<td>64 (27.2)</td>
<td>29.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Major depression</td>
<td>7 (5.1)</td>
<td>2 (3.3)</td>
<td>5 (21.7)</td>
<td>3 (21.4)</td>
<td>17 (7.2)</td>
<td>10.1</td>
<td>.001</td>
</tr>
<tr>
<td>Diagnostic subgroup of PD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td>70 (57.2)</td>
<td>34 (56.7)</td>
<td>12 (52.2)</td>
<td>6 (42.9)</td>
<td>131 (55.8)</td>
<td>2.2</td>
<td>.03</td>
</tr>
<tr>
<td>Probable</td>
<td>45 (36.2)</td>
<td>17 (28.3)</td>
<td>7 (30.4)</td>
<td>3 (21.4)</td>
<td>72 (30.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Possible</td>
<td>14 (10.2)</td>
<td>9 (15.0)</td>
<td>4 (17.4)</td>
<td>5 (35.7)</td>
<td>32 (13.6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Values are given as number (percentage). UPDRS indicates Unified Parkinson’s Disease Rating Scale; LL, linear-by-linear association test; and PD, Parkinson disease.

Table 3. Distribution of Patients With Different Stages of Parkinsonism According to UPDRS Thought Disorder Subscale Scores*  

<table>
<thead>
<tr>
<th>UPDRS Thought Disorder Subscale Score</th>
<th>No Disorder</th>
<th>Vivid Dreams</th>
<th>Hallucinations With Insight</th>
<th>Psychosis</th>
<th>Total Group (N = 235)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n = 37)</td>
<td>27 (19.5)</td>
<td>10 (16.7)</td>
<td>0</td>
<td>0</td>
<td>138 (100.0)</td>
</tr>
<tr>
<td>2 (n = 61)</td>
<td>59 (42.8)</td>
<td>17 (28.3)</td>
<td>5 (21.8)</td>
<td>0</td>
<td>60 (100.0)</td>
</tr>
<tr>
<td>3 (n = 59)</td>
<td>28 (20.3)</td>
<td>21 (35.0)</td>
<td>7 (30.4)</td>
<td>3 (21.4)</td>
<td>23 (100.0)</td>
</tr>
<tr>
<td>4 (n = 37)</td>
<td>20 (14.5)</td>
<td>8 (13.3)</td>
<td>4 (17.4)</td>
<td>5 (35.7)</td>
<td>14 (100.0)</td>
</tr>
<tr>
<td>Total Group</td>
<td>138</td>
<td>60</td>
<td>23</td>
<td>14</td>
<td>235</td>
</tr>
</tbody>
</table>

* Values are given as number (percentage). LL = 42.0; P < .001. UPDRS indicates Unified Parkinson’s Disease Rating Scale.

mous logistic regression, the nominal model option of program BMDP PR gave a log likelihood of −103.5 (goodness of fit χ², P = .20). The log likelihood when applying the ordinal model option was −104.7 (change in deviance, 2.4; P > .10 at 1 degree of freedom; goodness of fit χ², P = .25) and when applying the equal odds model option was also −104.7 (goodness of fit χ², P = .26). The equal odds model assumes that the odds ratios between adjacent outcome categories are the same across 2 distinct values of the independent variable, and a good fit indicates that log odds ratios are proportional to the difference in predictor score, ie, a linear relationship like that seen for a categorized interval-scaled variable.

With the equal odds model as a starting point, those variables previously shown to be significantly associated with the UPDRS thought disorder subscale score (Tables 1 and 2) were added 1 after the other in a stepwise, manual manner, checking for statistically significant reduction in deviance at each step. Neither dementia nor major depression contributed to explaining the thought disorder subscale score when the Hoehn and Yahr stage was already in the model. However, the MMSE score (cutoff points 18/19, 23/24, and 27/28) proved to be confounded with the Hoehn and Yahr stage, which was completely aliased by the MMSE score. There was a close relationship between the Hoehn and Yahr stage and the MMSE score. Among patients in Hoehn and Yahr stage 1 or 2, 12% had MMSE scores of less than 24, whereas among those
agents did not differ (\(n = 146\), 2 (\(n = 76\)), and 3 (\(n = 8\)) antiparkinsonism disorder subscale scores among patients treated with 1 vs 23.8), and had lower MADRS scores (8.6 vs 5.5) than (66.2 vs 74.9 years), had higher scores on the MMSE (28.2 score of 2 or more. However, these patients were younger treated with selegiline had a thought disorder subscale (Tables 1 through 3), the only independent explanatory variables were the MMSE, MADRS, and UPDRS Activities of Daily Living subscale score and the MADRS score, both introduced in the model as interval-scaled variables, reduced the deviance of the model significantly, whereas neither age (interval scaled) nor daily levodopa dose taken did (at cutoff points 300/301 mg and 600/601 mg daily), either alone or in combination with the MMSE score. Thus, among the variables related to the thought disorder subscale score, the only independent explanatory variables were the MMSE, MADRS, and UPDRS Activities of Daily Living scores.

**DRUG TREATMENT**

A total of 230 patients (97.9%) were using levodopa on January 1, 1993, with mean daily dose of 500 ± 238 mg. Only 5 patients (2.1%) were not taking antiparkinsonian agents owing to adverse effects (\(n = 3\)) or not being in need of symptomatic treatment (\(n = 2\)). The adverse effects that precluded the use of dopaminergic therapy were nausea (\(n = 1\)), psychosis (\(n = 1\)), and severe dementia and parkinsonism with a high risk for psychosis (\(n = 1\)). Mean age of the 5 patients not receiving dopaminergic therapy was 72.8 years (range, 61.0-86.0 years), and mean duration of PD was 5.2 years (range, 1.0-10.0 years). One hundred forty-three patients (60.9%) received levodopa only (mean daily dose, 465.0 ± 209 mg). Only 5 patients (2.1%) received anticholinergic agents in addition to levodopa; 52 patients (22.1%) were treated with the dopamine receptor agonist bromocriptine mesilate; and 37 patients (15.7%) were treated with selegiline hydrochloride, a selective monoamine oxidase type B inhibitor. Among the 2 latter groups, 2 patients received bromocriptine only and 1 patient received selegiline only, whereas the remaining patients received the drugs in conjunction with levodopa (mean daily levodopa dose, 551 ± 271 mg).

The thought disorder subscale scores were similar among patients treated with levodopa combined with other drugs compared with those receiving levodopa monotherapy (\(\chi^2 = 5.7; \ P = .2\)). Only 1 of 37 patients treated with selegiline had a thought disorder subscale score of 2 or more. However, these patients were younger (66.2 vs 74.9 years), had higher scores on the MMSE (28.2 vs 23.8), and had lower MADRS scores (8.6 vs 5.3) than those who did not receive selegiline. Similarly, thought disorder subscale scores among patients treated with 1 (\(n = 146\)), 2 (\(n = 76\)), and 3 (\(n = 8\)) antiparkinsonism agents did not differ (\(\chi^2 = 1.6; \ P = .6\)).

Nine patients were treated with an antipsychotic drug, and 31 patients were treated with antidepressant drugs. Reasons for antipsychotic therapy were delusions and hallucinations without insight associated with PD (\(n = 6\)), insomnia (\(n = 2\)), and anxiety (\(n = 1\)). At evaluation, 4 of 6 patients who received neuroleptic agents because of PD-associated psychosis were asymptomatic, whereas 2 patients reported hallucinations with insight. When these 6 patients were included in the psychosis group (thought disorder subscale score of ≥ 3), the proportion of psychotic patients was 8.5%. The relationship between psychosis and the clinical correlates analyzed above did not change when these 6 patients were included in the psychosis group.

**COMMENT**

This is the first population-based prevalence study of psychotic symptoms in PD. The study also provides insight into the determinants and the pathophysiological basis of delusional syndromes associated with PD. The frequency of hallucinations and delusions in patients with PD was found to be 16.0%, emphasizing their importance as clinical issues for patients with PD and their physicians. The high frequency of psychosis among institutionalized patients with PD calls attention to the imperative need to recognize and manage this complication in more severely disabled patients in advanced phases of their illness. The development of new antipsychotic drugs (ie, clozapine, olanzapine, remoxipride, risperidone, sertindole, quetiapine), more useful in this setting than conventional neuroleptic agents that may exacerbate parkinsonism, makes it possible to reduce these symptoms, relieve patient distress, and improve patient function once this source of behavioral disturbance is identified.

Care was taken to obtain the most complete case ascertainment. Because case ascertainment was based on patients with PD known by the health care system, possible unrecognized patients are absent from this study. However, all potential sources for patients with PD were scrutinized. The population in this part of Norway is characterized by a low level of migration, and the health care system is public. All patients with PD must see a neurologist to receive their first prescription of levodopa, and all neurologists practice at the district general hospital. A door-to-door survey would be the sampling method of choice, but it is reasonable to assume high case ascertainment in this study. Because patients with a history of psychosis before diagnosis of PD were excluded, the psychotic symptoms reported here probably represent a manifestation of PD or its treatment. Results of statistical analysis of the UPDRS thought disorder subscale suggest that a continuum of psychotic symptoms exists in PD. The UPDRS thought disorder subscale suggests a progression of psychotic symptoms, from vivid dreams via hallucinations to delusions. Our findings support this classification of psychotic phenomena in PD, in line with results of a previous investigation.

Use of dopaminergic and anticholinergic medications have traditionally been held responsible for psychosis in patients with PD because the prevalence of psychosis in patients with untreated PD is probably low. In this study, a complex relationship emerged between drug treatment and the occurrence of vivid dreams (1 on the thought disorder subscale), hallucinations (2 on the thought disorder subscale), and delusions (3 and 4 on the thought disorder subscale). Patients with vivid dreams were taking the highest levodopa doses, suggesting that this phe-
nomenon may be more closely related to drug dose. These patients were also significantly less demented and depressed than were patients with hallucinations and delusions. Thus, vivid dreams may be drug-induced phenomena, whereas the emergence of hallucinations and delusions occur in patients receiving levodopa therapy in the setting of dementia and depression. Failure to find a relationship between levodopa dose and hallucinations and delusions is in line with results of previous studies and has many possible explanations. First, only 5 patients were not treated with levodopa. Second, because this was a naturalistic study, the clinicians may have reduced levodopa administration in patients experiencing these symptoms. Third, host factors, such as cholinergic deficits in patients with dementia, may be a contributing circumstance.

The clinical correlates of hallucinations and delusions in patients with PD observed in this study suggest the mechanisms possibly responsible for these psychotic symptoms. Psychosis was more common in patients with possible PD than definite PD. This finding indicates that the presence of a non-PD parkinsonian disorder or atypical distribution of pathologic features in patients with PD is more likely to be associated with psychotic phenomena. A clinical diagnosis of dementia with Lewy bodies includes progressive cognitive decline, pronounced fluctuations of cognition, recurrent visual hallucinations, and parkinsonism. Some patients with possible PD, dementia, and hallucinations may have dementia with Lewy bodies, although this hypothesis was not supported by the results of a recent investigation. More research is needed to clarify the relationship between the dementia of PD with hallucinations and dementia with Lewy bodies. It is not yet clear whether it is correct to assume that a clear-cut distinction exists or whether the 2 disorders represent disorders on a continuum.

The relationship between cognitive impairment and disturbances of perception and thought was a compelling observation that emerged in this study. Patients with these symptoms had lower MMSE scores and were more likely to meet criteria for dementia than were patients without these symptoms. Results of previous studies demonstrate a similar relationship between hallucinations and dementia in patients with PD. There are several possible explanations for this relationship, including neurochemical and pathologic alterations. Atrophy of the nucleus basalis and consequent cholinergic deficits are more marked in demented than in nondemented patients with PD, and cholinergic deficits have been linked to psychosis in delirium, Alzheimer disease, and dementia with Lewy bodies. The cholinergic disturbance of dementia in patients with PD may thus contribute to the emergence of the psychosis. This hypothesis was supported by a preliminary study indicating that hallucinations and cognition improved in demented patients with PD who received cholinergic treatment.

Histological abnormalities may also contribute to the psychosis of PD. Recently, the occurrence of Lewy bodies in the cortex of patients with Parkinson disease was investigated. Cortical Lewy bodies are more prevalent in demented patients with PD, and the preferential paralimbic distribution of these changes positions them to contribute to psychosis and dementia. Some demented patients with PD have the pathologic changes of Alzheimer disease at autopsy examination, and there is a high prevalence of psychosis in patients with Alzheimer disease, suggesting that these changes might also increase the likelihood of psychosis. Thus, the link between psychosis and dementia might reflect a cholinergic deficit, cortical Lewy bodies, or Alzheimer-type cortical pathologic changes.

Patients with PD and hallucinations and delusions had more severe depressive symptoms than did those without. In most patients, the psychotic disorder lacked the features of psychotic depression (ie, delusions of guilt or illness), and the clinical syndromes seemed to be a combination of psychosis and mood changes. The psychotic features were similar in patients with and without depression. Depression in PD has been linked to deficits in serotonin and dopamine. The frequent co-occurrence of depression, psychosis, and dementia in patients with PD may indicate that with more widespread pathologic changes in the brain, it is more likely that systems critical to the occurrence of several types of psychopathologic changes will be affected. Alternately, interactions between multiple transmitter deficiencies in PD and dynamic changes in receptor sensitivity may create a neurochemical environment conducive to the emergence of delusional beliefs or depressive symptoms.

In summary, the present report comprises a unique epidemiological study of hallucinations and delusions in PD. Psychotic symptoms were found to be common, particularly in the late phases of the illness. Dementia, depression, more severe motor changes and atypical clinical features were all more common in patients with hallucinations and delusions, suggesting that more advanced and widespread brain changes involving several critical neurotransmitter systems underlie the emergence of psychotic symptoms in patients with PD. Abnormalities of cholinergic function and the presence of cortical or paralimbic Lewy bodies may be relevant to the occurrence of psychosis in patients with PD. The present study aids in identifying patients at greatest risk for psychotic symptoms and in anticipating which patients may be candidates for treatment with antipsychotic agents.

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REFERENCES

We invite submissions to the Images in Neurology section of the ARCHIVES. We invite your submission of interesting images of patients, tissue biopsy samples, and radiographic images, including magnetic resonance imaging, positive emission tomography, and x-ray scans, etc. With your image, please send a brief summary (300 words or less) describing its uniqueness and importance. Also, indicate the magnification and stain where appropriate. Both black-and-white and color images (at no charge to the author) are welcome. Submissions should be sent in triplicate to: Roger N. Rosenberg, MD, Editor, Archives of Neurology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75235-9108.

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