A Population-Based Investigation of Parkinson's Disease With and Without Dementia

Relationship to Age and Gender

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• Because the prevalence of idiopathic Parkinson's disease (PD) with or without dementia remains controversial, we initiated a population-based investigation in the Washington Heights–Inwood section of New York, NY, so that nearly complete case ascertainment could be achieved. A "registry" was developed for the study, and we advertised in periodicals and on radio and television. Subjects, or their records, were examined by experienced neurologists, and most underwent a battery of neuropsychological tests specifically designed for assessment in this community. All data were reviewed by a team of clinicians to achieve a consensus diagnosis. The crude prevalence of idiopathic PD, with and without dementia, was 99.4 per 100 000, increasing from 2.3 per 100 000 for those younger than 50 years to 1144.9 per 100 000 for those aged 80 years and older. The crude prevalence for PD with dementia alone was 41.1 per 100 000 and also increased with age from zero for those younger than 50 years to 787.1 per 100 000 for those aged 80 years and older. Prevalence ratios were comparable with those of other published population-based studies in similar settings. After standardization, men had PD with and without dementia more frequently than did women. The major difference between patients with and without dementia was a later estimated age at onset of motor manifestations. We conclude that PD is a frequent disorder in the elderly population that affects men and whites more frequently than women and nonwhites. Moreover, dementia in patients with PD is more frequent than previously recognized and is strongly related to the age at onset of motor manifestations.

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The prevalence of idiopathic Parkinson's disease (PD) has been estimated to be between 80.6[1] and 187.0[2] per 100 000 in the general population. The age-specific prevalence ratio increases dramatically with age. For example, in patients older than 65 years, the prevalence of PD is twice that for all lower age groups combined and doubles again after age 75 years.[3] At age 65 years and older, the prevalence of PD varies from 350 to 800 per 100 000. Both gender and racial differences have been reported,[4,5] but they are not consistent.[6] Some degree of variation in reports of prevalence may be due to an imprecise definition of idiopathic PD, resulting in the inclusion of patients with secondary parkinsonism.

The frequency of dementia in patients with idiopathic PD is also controversial. It is significantly more frequent in older patients,[7-13] particularly when motor manifestations begin after age 70 years.[9] Marttila and Rinne[10] and others[11,12] report the frequency of dementia in patients with PD to be 30%. However, Brown and Marsden[13] believe the frequency of dementia to be overestimated because of the lack of specific criteria for the diagnosis of dementia.

To overcome some of the methodologic issues of previous studies, we began a population-based study of PD and PD with dementia in the community of Washington Heights–Inwood in the northern part of the borough of Manhattan in New York, NY. We attempted complete case ascertainment in the region called Community District 12 (CD12), where, according to the 1980 census, 179 941 people reside, including nearly 35 000 elderly people (defined as persons older than 60 years). We used strict criteria for the diagnosis of idiopathic PD and for the diagnosis of dementia. Our objective was to estimate the population prevalence of PD with and without dementia in this geographically limited and culturally diverse area of northern Manhattan.

SUBJECTS AND METHODS

Subject Selection

To be included as a subject, all patients must have lived within the four zip codes identified as CD12 in Washington Heights–Inwood during the period of recruitment, which was from April 1, 1988, to December 31, 1990. Subjects were identified through the development of a "registry" for PD in the community for all individuals considered to have PD or a related disorder. This registry for PD included all patients seen at the Columbia Presbyterian Medical Center who resided in the community. Patients were identified from a series of sources: admission and discharge lists from the hospital, lists from various ambulatory care sites, contact with practitioners both in the hospital and in the community, and review of their charts. The *International Classification of Diseases, Ninth Revision* codes on computer-generated billing lists from various medical sources and registries of inpatients and outpatients at local medical centers were also used to identify subjects. Announcements were placed in every local newspaper for a 2½-year period around the time of the study. Both television

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and radio programs carried public announcements about the study during the same period. Private practitioners and the single neurologist in the community of Washington Heights–Inwood who is not affiliated with the medical center were also personally contacted. We were also given access to medical record information from the regional Health Insurance Providers in the upper part of Manhattan. A list of individuals with home health attendants was also obtained from the Health Resources Association and reviewed to identify patients with PD.

Using names and existing telephone numbers, subjects were contacted and asked to participate. Only those subjects able to give informed consent or who had a next of kin willing to grant informed consent on his or her behalf were fully examined in the course of our investigation.

Some individuals were identified through the registry but could not be examined for a number of reasons. The medical records of these individuals were reviewed by a neurologist (R.M.) to obtain appropriate clinical information. For the purpose of our investigation, we required that these patients have documented evidence in the record of having been examined during the prevalence period and that they meet the same inclusion and exclusion criteria for PD as the patients who were examined. When no information was found, the patient was contacted at the last known address or telephone number. Patients were considered "missing" when no information was available.

Inclusion Criteria

Idiopathic PD was defined as the primary form of the disease in which review of the medical history and physical signs indicated no other disease process that could be considered the cause of the disorder. Two of the following four cardinal features of PD must have been present on clinical examination or mentioned in the medical records: resting tremor, shuffling gait, bradykinesia, or muscular rigidity.

Exclusion Criteria

Patients were excluded if they had any of the following disorders: secondary or symptomatic parkinsonism (postencephalitic) or parkinsonism resulting from any of the following drugs: phenothiazines, alphamethyldopa, reserpine, or metaclopramide hydrochloride. Patients with progressive supranuclear palsy, essential tremor, Shy-Drager syndrome, presumed striatonigral degeneration, and olivopontocerebellar degeneration were also excluded, as were patients who developed memory loss or dementia before motor manifestations of PD and any patient considered to have the "extrapyramidal form" of Alzheimer's disease.[14]

Demographic Data

Information regarding current age, date of birth, location of birth, residence since birth, occupation, and duration of formal education was obtained in the initial interview or record review. For ethnic group assignment, the US Census Bureau format was used; a similar process is used by the hospital record system. Subjects were asked to which ethnic group they belonged and were given choices. We attempted to subdivide Hispanic patients into country of origin. (The questionnaire used is available from the authors upon request.)

Clinical Evaluation

Patients underwent a neurologic examination by one of three experienced neurologists (L.J.C., K.M., or R.M.). The presence and severity of motor signs and symptoms were recorded by the physician using the Unified Parkinson's Disease Rating Scale.[15] Current medications were listed in a semistructured format by a trained interviewer, as was the history of the current illness. If the patient was unable to give a history or appeared to be demented, the interview was conducted with the next of kin. Information regarding performance of activities of daily living was obtained during the same interview with part 1 of the Blessed Dementia Rating Scale[16] and the Schwab and England[17] rating scale of activities of daily living. All interviews were conducted in either Spanish or English, according to the patient's choice.

All patients underwent a complete neuropsychological assessment (also conducted in either Spanish or English, according to the patient's choice), which included the following tests: (1) orientation from the Modified Mini-Mental State Examination[18]; (2) the Selective Reminding Test[19]; (3) a multiple-choice version of the Benton Visual Retention Test (matching and recognition)[20]; (4) five selected items from the Rosen Drawing Test[21]; (5) 15 items from the Boston Naming Test[22]; (6) the Controlled Oral Word Association Test[23] and the Animal Naming[24] test; (7) selected items from the Comprehension and Repetition subtests from the Boston Diagnostic Aphasia Examination[24]; (8) the Similarities subtest from the Wechsler Adult Intelligence Scale–Revised[25]; and (9) Identities and Oddities from the Mattis Dementia Rating Scale.[26]

These neuropsychological tests were scored and compared with a series of cutoff scores developed in a pilot study of dementia in the community. The cutoff scores and their application to diagnosis have been described previously.[27] Briefly, demonstrable impairment in memory, and a similar degree of impairment in at least two other cognitive categories, including abstract thinking, constructional ability, language, and orientation, was required for a patient to meet criteria for dementia.[28] The impairment could not have resulted from delirium or an alteration in consciousness.

The evaluation of social or occupational function, also required for the diagnosis of dementia,[28] was made with use of the Activities of Daily Living measures and medical history. We separated functional impairment due to intellectual dysfunction from that due to physical impairment. At the consensus conference, all the information derived from the neurologic examination and that derived from neuropsychological assessment were reviewed by a group of physicians and neuropsychologists, some of whom were involved in the assessment of the patient. For all dementia diagnoses, a consensus among the reviewers was required.

The diagnosis of idiopathic PD and dementia in the 22 patients not examined was made from a review of the records. For the diagnosis of idiopathic PD, we used the same inclusion and exclusion criteria. However, we required the diagnosis to have been made and entered into the medical records by the attending physician. In every case, this attending physician was a neurologist. For dementia, we required written evidence in the records of a history of intellectual impairment, verified by a neurologic examination or neuropsychological tests. For both diagnoses, we required that they had not been retracted or changed in subsequent entries in the medical record.

Database Management and Statistical Analysis

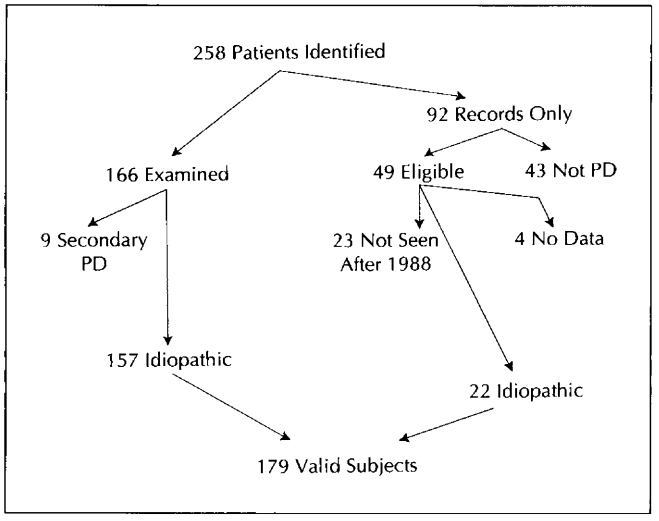
All data were entered by the data entry clerk and periodically checked by the project coordinators. Data were stored with the use of the Scientific Information Retrieval database management software. Analytic methods consisted primarily of calculations of rates and proportions.[29,30] To compare the prevalence of idiopathic PD between men and women and among ethnic groups, as well as to compare our data with those of other studies, indirect standardization was used.[30] We calculated standardized prevalence rates by weighting each age group based on the proportion of the age group in the total population according to the 1988 US Department of Commerce Bureau of Census estimates.[31] Each comparison between gender, ethnicity, or studies was expressed as a standardized rate ratio, defined as the ratio of the standardized prevalence rate in one group to that in another.

RESULTS

Parkinson's Disease

A total of 258 cases of presumed parkinsonism were identified by the registry, from which we determined that 179 cases (71%) were the idiopathic form of PD. The flow diagram shown in the Figure traces patient ascertainment. A total of 166 patients (64%) were examined by one of us

to verify diagnosis, but only 157 were found to have idiopathic PD. The other nine patients were deemed to have secondary forms of parkinsonism. Among the 92 cases that were limited to record review, we identified 49 patients meeting inclusion criteria. The remaining 43 patients had either secondary parkinsonism (n = 15) or other disorders (n = 22); in six patients, no clinical information was available to determine diagnosis. Among the 49 eligible cases, only 22 had been examined during the prevalence period; four others were known by us to be cases, but no information was available, and 23 were not seen after April 1, 1988. Thus, the total number of valid cases for this study identified by the two methods was 179 (157 examined cases and 22 records reviewed). The remaining analyses and discussion are based only on information derived from this group of patients with idiopathic PD. Their demographic characteristics are summarized in Table 1.



Ascertainment of cases for investigation. PD indicates Parkinson's disease.

A total of 41.3% of these patients were found to have dementia during the prevalence period. Table 1 shows the demographic characteristics of the patients with and without dementia.

According to the 1980 census, 179 941 people resided in northern Manhattan. The total number of individuals in this community did not change significantly by the 1990 census, remaining within 3% of the 1980 figures. The crude prevalence of PD as of the midpoint date (July 1, 1989) was 99.48 per 100 000 persons. For the group 35 years and older, the crude prevalence was 219.8 per 100 000. The age-specific prevalence increased dramatically with age from 2.3 per 100 000 for those younger than 50 years to 1144.9 per 100 000 for those older than 80 years (Table 2). The proportion of those with dementia is presented in Table 2.

The age-specific prevalence in the community was standardized to the 1988 US census estimates.[31] There were 191.2 cases per 100 000 in the population aged 35 years and older and 86.9 cases per 100 000 for all age groups. For comparison, the standardized age-specific prevalence is shown in Table 3 for two similar studies—one in Northampton, England,[32] and the other in Copiah County,

Table 1.—Demographic Characteristics of Patients With Parkinson's Disease in Washington Heights–Inwood*

Variable	Patients: Without Dementia (n = 105)	Patients: With Dementia (n = 74)	Total (N = 179)
Mean (SD) age, y	71.75 (10.1)	79.41 (7.79)†	74.92 (9.91)
% Women	51.4	51.4	51.4
Mean (SD) duration of symptoms, y	5.92 (6.22)	5.68 (5.43)	5.83 (5.92)
Mean (SD) years of education	10.05 (4.7)	9.05 (4.8)	9.63 (4.76)
% Black (not Hispanic)	4	14	8
% Hispanic	45	39	43
% White (not Hispanic)	51	47	49

*Data include all patients examined and those from record review. Washington Heights–Inwood is a community in Manhattan, NY.
†$P < .001$.

Table 2.—Prevalence of Parkinson's Disease (PD): Crude Ratios of Patients With and Without Dementia in Washington Heights–Inwood*

Age Group, y	Crude Prevalence†: PD Total	Crude Prevalence†: PD With Dementia	Proportion Demented	Population Base (1980)
<50	23 (3)	0 (0)	0	128 148
50-59	45.7 (8)	5.7 (1)	0.124	17 468
60-69	234.8 (38)	55.6 (9)	0.236	16 179
70-79	525.6 (66)	159.2 (20)	0.302	12 556
>80	1144.9 (64)	787.1 (44)	0.687	5590
All ages	99.4	41.1 (74)	0.413	179 941

*Washington Heights–Inwood is a community in Manhattan, NY.
†Values are per 100 000. Numbers in parentheses indicate numbers of patients.

Mississippi.[6] Standardized rate ratios were calculated for the comparisons between these two studies and ours (Table 3). As is apparent, the standardized age-specific prevalences differ primarily in the younger patients.

We also calculated crude prevalence ratios for different ethnic groups in the Washington Heights–Inwood sample. We assumed that there might be an increase in the number of Hispanic residents relative to white and black residents due to shifts in the proportions of the population during the 1980s. Therefore, the 1980 census data with regard to ethnic groups would underestimate the Hispanic population in the community and overestimate the white population. Because 1990 census data were not available for these comparisons, we corrected for this by estimating the current ratio of the three ethnic groups in the community from data available to us through Medicare registration in 1989 and through our own survey of more than 2500 subjects participating in a community-based study of neurologic disorders. Based on data from these sources, of individuals older than 60 years, 35.3% were black, 37.4% were Hispanic, and 21.3% were white. The overall crude prevalence ratios for blacks was 107.3 per 100 000, for Hispanics was 521.6 per 100 000, and for whites was 1176.8 per 100 000. We did not standardize these estimates because of the uncertainty of the denominator information. Therefore, any comparison between ethnic groups at this time would be misleading. We anticipate age-specific denominator information by ethnic group to be available in the spring of 1992.

The comparison of prevalence in men and women indicated a 73% increase in the standardized prevalence for PD with and without dementia for men in nearly every age group. There was an 87% increase in the standardized prevalence of PD with dementia in men (Table 4).

Parkinson's Disease With Dementia

The overall crude prevalence of PD with dementia was 41.1 per 100 000, and the crude prevalence for those individuals older than 35 years was 90.8 per 100 000 (Table 2). The age-specific prevalence of PD with dementia also increased with age, parallel to the increase in PD overall, as noted in Table 2, from zero per 100 000 for those younger than 50 years to 787.1 per 100 000 older than 80 years. The standardized prevalence ranged from 5.3 per 100 000 for those between ages 35 and 64 years to 62.5 per 100 000 for those older than 75 years (Table 5). The standardized rate ratio for dementia was 0.39 overall, as noted in Table 5. Demented patients were older than their nondemented peers, but duration of motor manifestations was identical (Table 1). To compare the prevalence of PD with demen-

Table 3.—Comparison of Standardized, Age-Specific Prevalence Ratio of Parkinson's Disease in New York, Mississippi, and the United Kingdom*

Age Group, y	Washington Heights–Inwood†	Mississippi and United Kingdom	Standardized Rate Ratio
	Copiah County, Miss (6)		
40-64	39.8	93.0	0.43
65-74	43.2	87.9	0.49
75+	106.8	105.3	1.01
Total	191.2‡	286.3‡	0.66
	Northhampton, UK (32)		
<50	1.7	2.2	0.78
50-59	4.1	8.2	0.50
60-69	20.1	24.4	0.83
70-79	29.9	47.9	0.62
>80	30.9	34.9	0.88
Total	86.9‡	117.8‡	0.78

*Data are standardized to the US census estimate for 1988 (US Department of Commerce[31]).
†Washington Heights–Inwood is a community in Manhattan, NY.
‡Data are per 100 000.

Table 4.—Comparison of Standardized Prevalence Ratio for Parkinson's Disease (PD) With and Without Dementia by Gender

	PD in Men*		PD in Women*			
Age Group, y	Total	Dementia Only	Total	Dementia Only	SRR, Total†	Men/Women With Dementia Only
<50	1.2	0	2.2	0	0.55	0
50-59	8.5	1.2	0.8	0	9.50	0
60-69	33.1	9.6	12.1	1.7	2.73	5.68
70-79	33.7	11.2	27.7	7.8	1.21	1.43
>80	42.4	28.8	25.5	17.7	1.66	1.63
Total	119.0	50.9	68.5	27.2	1.73	1.87

*Data are per 100 000.
†SRR indicates standardized rate ratio.

Table 5.—Standardized Rate Ratio of Dementia in Parkinson's Disease (PD): Washington Heights–Inwood*

Age Group, y	Standardized Prevalence of PD†	Standardized Prevalence of PD and Dementia†	Standardized Rate Ratio (PDD‡ to PD)
35-64	41.1	5.3	0.12
65-74	43.2	8.2	0.19
75+	106.8	62.5	0.59
Total	191.2	76.0	0.39

*Data are based on US census estimates for 1988. Washington Heights–Inwood is a community in Manhattan, NY.
†Data are per 100 000.
‡PDD indicates PD with dementia.

tia with that of clinically diagnosed Alzheimer's disease, we used the age-specific prevalence ratios from the Eastern Baltimore Mental Health Survey.[33] We found a standardized rate of clinically diagnosed Alzheimer's disease in that study to be 550 per 100 000 compared with the standardized rate of PD with dementia in our study of 70.7 per 100 000.

COMMENT

We found that the age-specific prevalence ratio of PD increases dramatically with age, as has been reported by other investigators.[1-3,6,32] Furthermore, we believe our study to be one of the few population-based estimates of dementia in patients with PD. The overall frequency of dementia was 41.3%, much higher than expected based on earlier studies.[7-13] The proportion of patients with dementia also increased with age, as did the age-specific prevalence of PD with dementia. However, the standardized rate ratio for clinically diagnosed Alzheimer's disease was still nearly eight times that for PD with dementia in our investigation.

We confirmed the increased prevalence of PD in men relative to women and found a similar relationship for PD with dementia. Our data regarding the prevalence of PD in each ethnic group suggests that whites are more frequently affected than are either blacks or Hispanics, but this was based on estimates of the distribution of each ethnic group and requires confirmation when appropriate data are available from the 1990 census. Moreover, any differences in prevalence should be confirmed with incidence data to reduce "prevalent case bias."[31] As with any prevalence or cross-sectional investigation, our collected data should be interpreted with caution.

How Complete Was Case Ascertainment in the Washington Heights–Inwood Community?

Because the community is a relatively small geographic area with a single hospital in the region, we believe that the sample represents a nearly complete sample. Our estimate may be lower than that in Copiah County[6] and Northhampton[32] because we used very strict criteria for the diagnosis of PD. Still, our estimate of prevalence was similar to those of studies that used different methods of case ascertainment.[1,6,32] During the course of our study, we were fortunate to have access to a survey of 700 elderly (older than 65 years) members of our target community who were receiving home assistance from the Health Resources Association. Of the 28 cases of PD identified in that survey, only three patients were previously unknown to us. This suggests that our case-ascertainment in that particular region of the community was as complete as was possible in an urban area. We also reviewed clinic records from the adjacent community of Harlem and found only two eligible cases for our study.

Our estimate of the prevalence of PD was somewhat lower than expected based on published rates in the studies from Northhampton[32] and Copiah County,[6] except in the older age groups. This may reflect differences in methods of recruitment as well as our stricter criteria for the diagnosis of PD.

We observed fewer cases of PD among Hispanics and blacks than among whites. The prevalence ratios may "artificially" differ among the three ethnic groups because of the apparent change in the proportions each group represents in the current population.

Was There a Selection Bias in the Identification of Cases?

We cannot identify a systematic bias in the identification of cases in our study. Patients were identified during a 2½-year period. It is possible that patients with more advanced illness were more easily identified by the methods we used, which would have increased the number of patients with dementia. However, we have no indication that this occurred, because all cases were identified with similar methods of surveillance.

Was the Definition of Parkinson's Disease and Dementia Adequate and Appropriate?

According to Rajput et al,[34] the accuracy of a clinical diagnosis of PD may be as low as 76%, which would make epidemiologic studies difficult. Rajput et al also noted that this figure improved when patients were followed up for a period of 5 years or more[34] and when multiple examiners were used. By requiring two defining features, we were assured of the identification of "typical" cases, although we may have missed subtle or very mild cases of idiopathic PD. We believe that we were able to exclude essential tremor and secondary forms of parkinsonism, which may also explain why our overall prevalence was lower than that in the other two studies cited, because their criteria were not as strict. When the diagnosis was in question, the other neurologists participating in the study were asked to examine the patient, and a consensus was reached.

The diagnosis of dementia is difficult in our community because the educational level varies considerably, and educational level may affect performance on neuropsychological tests. We used a two-stage approach to the diagnosis. First, the neurologist made a decision based on the medical history, the ability to perform activities of daily living, the results of a neurologic examination, and a brief assessment of mental status. Second, the neuropsychological testing was performed on the same date but independently. The battery of neuropsychological tests had been developed and tested in the community before its application in this project.[27] All information derived from these interviews was used in a consensus conference attended by all investigators to determine the final diagnosis. To reduce education bias, our diagnostic criteria for dementia required that a patient exhibit impairment in performing the activities of daily living that were directly related to cognitive decline. A patient who performed poorly on neuropsychological tests but was able to function independently was not considered to be demented. Thus, while we may not have fully eliminated bias in diagnoses with regard to dementia, we believe that we reduced bias to a minimum.

How Common Is Dementia in Parkinson's Disease?

In 1984, Brown and Marsden[13] challenged colleagues by positing that the frequency of dementia in the majority of studies published at that time had been overestimated. They found inconsistencies in the criteria for the diagnosis of PD and dementia and identified a number of potential problems that could obscure the diagnosis of dementia in PD. Their review of investigations performed during the last 60 years indicated an estimate of between 35% and 90%, but they intimated that when *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition* criteria[28] for dementia were applied, a lower estimate of 15% would better reflect the actual frequency of dementia. Their report was supported by subsequent studies.[35,36]

Strict criteria for PD and for dementia would improve the accuracy of estimates of their frequency. In addition, unless the population from which patients are selected is specified, prevalence estimates might simply reflect a selection bias from a particular hospital or clinic. In the single community-based study, Sutcliffe[32] found an 11% prevalence rate for dementia in PD in Northhampton but failed to use precise diagnostic criteria.

Rajput et al[3] found the cumulative probability of patients with PD developing dementia to be 21.1% compared with 5.7% for the healthy controls in a retrospective chart review. In our own clinic- and hospital-based investigation,[9,37] the cumulative risk of dementia in patients with idiopathic PD was 60% by age 85 years. These investigations need to be confirmed in "population-based" prospective studies.

Parkinson's disease is a common degenerative disease of the nervous system. Our study indicates that it is more frequent in the elderly and progresses dramatically with increasing age. We also found the expected differences in gender and evidence for differences in prevalence in the black and Hispanic populations.

With regard to dementia, we report the first population prevalence ratio for dementia in patients with idiopathic PD: 41.3%. We also confirm earlier work that indicates that PD with dementia is clearly age dependent, and its frequency increases with each decade of life. The prevalent cases with and without dementia differed in age but not duration of illness (motor manifestations). This strongly suggests that age at onset of PD influences the prevalence of dementia. Confirmation of these data awaits studies of incidence rates of PD with and without dementia.

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