Importance The frequency and distribution of synucleinopathies and tauopathies manifesting with parkinsonism in the general population are poorly understood, thus affecting health care planning and research.

Objective To investigate the incidence and distribution of specific types of parkinsonism and related proteinopathies.

Design We used the medical records–linkage system of the Rochester Epidemiology Project to identify all subjects who received a screening diagnostic code related to parkinsonism in Olmsted County, Minnesota, from January 1, 1991, through December 31, 2005 (15 years). A movement disorders specialist reviewed the complete medical records of each subject who screened positive to determine the type of parkinsonism and the presumed proteinopathy using specified criteria.

Setting Geographically defined population.

Participants All residents of Olmsted County who provided authorization to use their data for medical records research (population-based sample).

Main Outcome and Measures Incidence of parkinsonism and specific proteinopathies.

Results Among 542 incident cases of parkinsonism, 409 (75.5%) were classified as proteinopathies. Of the 389 patients with presumed synucleinopathies (71.8%), 264 had Parkinson disease (48.7% of all cases). The incidence rate of synucleinopathies was 21.0 per 100,000 person-years overall and increased steeply with age. The incidence rate of tauopathies was 1.1 overall (20 cases), and the most common tauopathy was progressive supranuclear palsy (16 cases). Thirty-six subjects had drug-induced parkinsonism (6.6%), 11 had vascular parkinsonism (2.0%), 1 had amyotrophic lateral sclerosis in parkinsonism (0.2%), 1 had parkinsonism secondary to surgery (0.2%), and 84 remained unspecified (15.5%). Men had a higher incidence than women for most types of parkinsonism. Findings at brain autopsy confirmed the clinical diagnosis in 53 of 65 patients who underwent autopsy (81.5%).

Conclusions and Relevance The incidence of proteinopathies related to parkinsonism increases steeply with age and is consistently higher in men than women. Clinically diagnosed synucleinopathies are much more common than tauopathies. Findings at autopsy confirm the clinical diagnosis of presumed proteinopathy. Our findings may guide health care planning and prompt new research directions.

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In the United States, as in many countries worldwide, life expectancy has increased dramatically in the past century. With the proportionately older population, more persons are expected to develop neurodegenerative disorders. A recent study estimated that the prevalence of Parkinson disease (PD) and related disorders will increase dramatically in the next few decades.1

Several studies assessed the incidence of PD and other parkinsonisms.2-4 Although all the studies confirmed that PD is the most common,2 the data regarding other types of parkinsonism remain limited because the diagnosis is difficult and the diseases are relatively rare.5-6 Neurodegenerative conditions have now been classified on the basis of the presumed underlying protein substrates. Because α-synuclein is the predominant protein associated with PD, other Lewy body disorders, and multiple system atrophy (MSA), these conditions have been termed synucleinopathies.7-8 Similarly, parkinsonisms thought to be related to microtubule-associated tau protein have been termed tauopathies.9 This group includes progressive supranuclear palsy (PSP) and many cases of corticobasal syndrome (CBS). In this study, we investigated the incidence and the distribution by age and sex of clinically diagnosed proteinopathies related to parkinsonism in a well-defined population during a 15-year period. For a subsample of our patients, we were able to validate our clinical diagnosis at autopsy.

Methods

Study Population

We studied the geographically defined population of Olmsted County, located in southeastern Minnesota, from January 1, 1991, through December 31, 2005 (incidence study period of 15 years). Extensive details about the Olmsted County population have been reported elsewhere.10-13 This study was approved by the institutional review boards of the Mayo Clinic and Olmsted Medical Center, Rochester, Minnesota. Written informed consent was not required for passive medical record review.11

Case Ascertainment

We ascertained cases of parkinsonism through the records-linkage system of the Rochester Epidemiology Project. This system provides the infrastructure for indexing and linking essentially all medical information of the county population.10-13 All medical diagnoses, surgical interventions, and other procedures are entered into computerized indexes using codes from the Hospital Admission of the International Classification of Diseases, Eighth Revision,14 or the International Classification of Diseases, Ninth Revision.15

We ascertained potential cases of parkinsonism in 2 phases, including computerized screening and clinical confirmation. In phase 1, we searched the indexes for 38 diagnostic codes, including 5 for PD, 14 for parkinsonism, 7 for tremor, 2 for extrapyramidal disorders, 5 for nonspecific neurodegenerative diseases, 2 for MSA, and 3 for PSP. These 38 codes were the smallest subset that completely captured all cases of parkinsonism in a previous study of the incidence of parkinsonism performed in the same population from 1976 to 1990 (the list is given in the eTable in Supplement). This list of 38 codes was designed to yield maximum sensitivity at the cost of low specificity because the clinical confirmation phase was relatively rapid and did not involve the participants (no burden to study subjects).

In phase 2, a movement disorders specialist (R.S.) reviewed the complete records of all persons who received at least 1 of these diagnostic codes during the 15-year incidence study period or during the following 5 years using a specifically designed data abstraction form that was computerized for direct data entry (clinical confirmation phase). We extended the search for incident cases of parkinsonism for 5 years after the incidence study period (January 1, 2006, through December 31, 2010) to ensure that persons with a delayed diagnosis could be counted correctly. The movement disorders specialist defined the approximate date of onset and the type of parkinsonism using specified diagnostic criteria and following a manual of instructions (Table 1).6,16-20 Onset of parkinsonism was defined as the approximate date on which 1 of the 4 cardinal signs of parkinsonism was first noted by the patient, by family members, or by a care provider (as documented in the medical record).

Diagnostic Criteria for Parkinsonism and Proteinopathies

Our diagnostic criteria included the definition of parkinsonism as a syndrome and the definition of types of parkinson-
ism within the syndrome. Parkinsonism was defined as the presence of at least 2 of the following 4 cardinal signs: rest tremor, bradykinesia, rigidity, and impaired postural reflexes. Among the persons who fulfilled the criteria for parkinsonism, we applied the diagnostic criteria listed in Table 1 to classify the type of parkinsonism. In addition, we used clinical characteristics to group patients with parkinsonism into those with presumed synucleinopathies or presumed tauopathies.7–9 Synucleinopathies included PD, parkinsonism with dementia, and MSA.7,8 Tauopathies included PSP and CBS.9

Patients with uncertain underlying proteinopathy were included in the category “other types of parkinsonism.” This category included patients who did not have enough clinical information to fulfill the criteria for a particular type of parkinsonism (ie, parkinsonism unspecified) and patients with types of parkinsonism not associated with a specific pathological hallmark (eg, drug-induced parkinsonism, vascular parkinsonism, and secondary parkinsonism).

Reliability and Validity of Diagnosis and Classification
To study the reliability of our case-finding procedure, 40 records reviewed by the primary movement disorders specialist (R.S.) were independently reviewed by a second movement disorders specialist (J.H.B.) who was kept unaware of the initial diagnosis. The 40 records were selected randomly among those classified by the primary neurologist as parkinsonism (15 records), PD (15 records), and parkinsonism excluded after screening positive (10 records). Agreement on the presence of parkinsonism or PD was 90.0% (27 of 30 records). The 3 disagreements involved cases diagnosed as PD, drug-induced parkinsonism, or vascular parkinsonism by the primary neurologist and excluded by the second neurologist. Agreement on the exclusion of parkinsonism in subjects who screened positive was 70.0% (7 of 10). The 3 disagreements involved cases found to be PD, drug-induced parkinsonism, and parkinsonism unspecified by the second neurologist.

For the 27 subjects found to be affected by parkinsonism by both neurologists, the agreement was 74.1% (20 of 27) for PD vs other type of parkinsonism and 85.2% (23 of 27) for synucleinopathy vs other type. Finally, for the subjects found to be affected by parkinsonism by both neurologists, the agreement on year of onset of symptoms was within 1 year in 21 subjects (77.8%) and within 3 years for 26 of the 27 subjects (96.3%). In general, the agreement regarding the year of onset was high (intraclass correlation coefficient, 0.85 [95% CI, 0.77–0.92]).21

To validate the classification in presumed synucleinopathies and tauopathies, we reviewed the autopsy reports for all the patients who died during the study and for whom an autopsy was available. Detailed results of the validation study are reported in the Results section.

Statistical Analysis
We excluded subjects who denied authorization to use their medical records for research.20 All individuals who met criteria for parkinsonism with symptom onset from January 1, 1991, through December 31, 2005, and who were residents of Olmsted County at the time of symptom onset were included as incident cases. We calculated incidence rates using incident cases as the numerator and population counts from the Rochester Epidemiology Project Census as the denominator.11 The denominator was corrected by removing prevalent cases of parkinsonism estimated using prevalence figures from several European populations.22 Details about this correction were published elsewhere.5

We computed age- and sex-specific incidence rates for parkinsonism overall, for specific types of parkinsonism, and for specific proteinopathies. Because our study was descriptive and involved the entire Olmsted County population, no sampling procedures were involved and statistical tests were not necessary for the interpretation of the data.23

Results
We identified 5505 individuals with at least 1 screening code of interest from 1991 through 2010. We excluded 400 individuals because they were not residents of Olmsted County at the time of symptom onset and 136 persons because they did not give permission to use their medical records for research. Of the 4969 remaining persons, 3877 were found to be not affected by parkinsonism at record review, 12 lacked sufficient clinical documentation to determine their parkinsonism status, 374 had onset of parkinsonism before January 1, 1991, and 164 persons had onset after December 31, 2005. In summary, we included 542 incident cases of parkinsonism with onset from January 1, 1991, through December 31, 2005. Only 35 persons (6.5%; 18 with PD) received a first screening diagnostic code after December 31, 2005, but had the onset of parkinsonism retrodated to within the study period (1991-2005).

Table 2 shows the age- and sex-specific incidence rates for presumed synucleinopathies, presumed tauopathies, and other types of parkinsonism. The Figure shows the age- and sex-specific incidence rates of all parkinsonisms, PD, synucleinopathies, and tauopathies. Of the 542 patients identified, 389 (71.8%) had clinically presumed synucleinopathies, 20 (3.7%) had clinically presumed tauopathies, and 133 (24.5%) had other types of parkinsonism (Table 2). The overall incidence rate for parkinsonism of all types was 29.3 cases per 100 000 person-years. Incidence rates increased sharply with age from 97.9 at 60 to 69 years to 304.8 at 80 to 99 years (Figure).

Synucleinopathies
The incidence rate of synucleinopathies was 21.0 (per 100 000 person-years) overall, was higher in men (27.0) than in women (15.4), and increased steeply with age. We identified 264 patients with PD, 110 with parkinsonism with dementia, and 15 with MSA. Parkinson disease was the most common type of synucleinopathy and was more frequent in men than in women (62.9% of PD cases were men). The incidence rate was higher in men than in women for all synucleinopathies (Figure).

Tauopathies
Presumed tauopathies manifesting as parkinsonism were uncommon, with a total of 20 patients (11 men and 9 women) and an overall incidence of 1.1 cases per 100 000 person-years. All
patients with presumed tauopathies had onset of symptoms at 60 years or older. The most common tauopathy was PSP, with incidence higher in men than in women (1.1 vs 0.6). Corticobasal syndrome was more frequent in women (3 cases) than in men (1 case) and had an overall incidence of 0.2 per 100,000 person-years (0.1 in men and 0.3 in women) (Figure).

### Other Parkinsonism

We identified 36 patients with drug-induced parkinsonism, 11 with vascular parkinsonism, 1 with amyotrophic lateral sclerosis in parkinsonism, 1 with atypical parkinsonian syndrome, 1 with multiple system atrophy, and 1 with parkinsonism secondary to cingulotomy. This group included 1 patient with amyotrophic lateral sclerosis in parkinsonism who carried a repeat expansion in the noncoding region of chromosome 9.

### Table 2. Incidence Rates of Specific Types of Parkinsonism and Proteinopathies in Olmsted County, Minnesota, 1991-2005

<table>
<thead>
<tr>
<th>Type of Parkinsonism</th>
<th>Incidence Rate per 100,000 Person-Years (No. of Cases)</th>
<th>Age Group, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any parkinsonism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.2 (1)</td>
<td>4.2 (24)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>2.7 (8)</td>
</tr>
<tr>
<td>Synucleinopathies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>3.2 (9)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.7 (2)</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>1.1 (9)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.7 (2)</td>
</tr>
<tr>
<td>Parkinsonism with dementia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Tauopathies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Progressive supranuclear palsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>3.2 (3)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>1.2 (1)</td>
</tr>
<tr>
<td>Corticobasal syndrome</td>
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<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Other types of parkinsonism^a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.2 (1)</td>
<td>2.3 (13)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>2.0 (6)</td>
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<tr>
<td>Drug-induced parkinsonism</td>
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<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.1 (1)</td>
<td>1.0 (6)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>1.1 (3)</td>
</tr>
<tr>
<td>Vascular parkinsonism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Parkinsonism unspecified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0.1 (1)</td>
<td>1.1 (3)</td>
</tr>
<tr>
<td>Women</td>
<td>0.0 (0)</td>
<td>0.7 (2)</td>
</tr>
</tbody>
</table>

^a Incidence rates can be computed by dividing the number in parentheses by the corresponding denominator and multiplying by 100,000. Denominators in person-years for men and women combined were as follows: ages 0 to 29 years, 843,999; ages 30 to 49 years, 577,614; ages 50 to 59 years, 180,689; ages 60 to 69 years, 116,489; ages 70 to 79 years, 80,829; ages 80 to 99 years, 53,142; and all ages, 1,852,762. Denominators for men were as follows: ages 0 to 29 years, 418,326; ages 30 to 49 years, 277,387; ages 50 to 59 years, 86,452; ages 60 to 69 years, 55,288; ages 70 to 79 years, 34,695; ages 80 to 99 years, 16,155; and all ages, 888,303. Denominators for women were as follows: ages 0 to 29 years, 425,673; ages 30 to 49 years, 300,227; ages 50 to 59 years, 94,237; ages 60 to 69 years, 61,201; ages 70 to 79 years, 46,134; ages 80 to 99 years, 36,987; and all ages, 964,459.

^b This group included 1 patient with amyotrophic lateral sclerosis in parkinsonism who carried a repeat expansion in the noncoding region of chromosome 9. In addition, this group included 1 patient with parkinsonism secondary to cingulotomy.
kinsonism. The overall incidence of other types of parkinsonism was higher in men than in women (7.8 vs 6.6). Unspecified parkinsonism and vascular parkinsonism were more common in men, whereas drug-induced parkinsonism was more common in women (Table 2).

Pathological Validation of Clinical Diagnoses

Of the 542 incident cases of parkinsonism, 343 (63.3%) had died by December 31, 2011, and 65 (19.0% of deceased patients) had a brain autopsy available for review (Table 3). The pathology observed at autopsy was consistent with the type of proteinopathy that was presumed clinically in 53 patients (81.5%). The concordance was 80.4% for synucleinopathies (45 of 56 cases), 100.0% for tauopathies (2 cases with CBS), and 85.7% for other parkinsonisms (6 of 7). Of the remaining 11 patients presumed to have a synucleinopathy at clinical diagnosis, 3 had tau pathology and 8 had nonspecific age-related changes (6 of these 8 cases had incontinence of the substantia nigra without evidence of Lewy bodies or tau pathology). Of the 7 patients with other parkinsonisms, 1 had Lewy body pathology. None of the brains exhibited comorbid Lewy body pathology and tau pathology.

Discussion

Our study suggests that clinically presumed synucleinopathies are the most common type of parkinsonism, and PD is the most common synucleinopathy. The second most common synucleinopathy is parkinsonism with dementia, followed by MSA. The incidence of all synucleinopathies increases steeply with age and is higher in men than women. The incidence of all tauopathies increases after 60 years of age, and men have higher incidence than women, except at the ages of 80 to 99 years. Progressive supranuclear palsy is the most common tauopathy, followed by CBS. For a subsample of our patients, we were able to validate our clinical diagnosis at autopsy (65 incident cases; 12.0% of all cases and 19.0% of deceased cases).

Several studies of the incidence of parkinsonism or PD have been published; however, to our knowledge, no population-based studies have examined the incidence of clinically presumed proteinopathies. Previous studies have found that PD is the most common type of parkinsonism. Age- and sex-standardized incidence rates for PD have been reported in the

Incidence is calculated per 100,000 person-years. A, All parkinsonism. B, Parkinson disease (PD). C, Synucleinopathies. D, Tauopathies. The scale for incidence was reduced for tauopathies (the y-axis values range from 0 to 25 per 100,000 person-years).
range of approximately 10 to 18 cases per 100 000 person-years (rates adjusted to the 1990 US Census population). On set of PD is uncommon before 60 years of age, and the incidence of PD and other types of parkinsonism increases steeply after 60 years of age.

In our study, PD and most other types of parkinsonism were more common in men than in women. This pattern is consistent with a number of studies that showed a higher incidence of PD in men than women. In addition, some studies reported sex differences in clinical and preclinical characteristics and in risk factors for PD. Genetic, endocrinologic, environmental, or social and cultural differences may explain the differences in the risk of PD between men and women.

Findings from this investigation were consistent with results from a previous study in the same Olmsted County population. The overall age- and sex-adjusted incidence rate for PD was 16.5 in the current study and 14.2 in 1976 through 1990 (both rates adjusted to the 1990 US Census population). In addition, we found consistent patterns of incidence by age and sex. However, we also found small differences. For example, Bower et al reported no cases of CBS in the 1976-1990 study, probably because CBS was not adequately recognized at the time. Our study has a number of strengths. First, taking advantage of the records-linkage system of the Rochester Epidemiology Project, we studied a large and well-defined population (1 852 762 person-years overall). Second, because our study included 542 incident cases of parkinsonism, we were able to explore the distribution of clinical types of parkinsonism by age and sex. In addition, we were able to group incidence cases by presumed proteinopathy. Third, 63.3% of cases were followed up from the onset of parkinsonism to the time of death, and 94.3% were followed up through death or for at least 5 years after onset. This long follow-up provided information on the natural history of the disease and strengthened the classification by type of parkinsonism.

Fourth, all cases were adjudicated by a movement disorders specialist at the time of medical records abstraction to reduce differences in the diagnostic criteria over time or across the different care professionals (nurses, generalists, or specialists). Fifth, all medical facilities in Olmsted County are included in the Rochester Epidemiology Project, and a patient living in the county is unlikely to have been seen for parkinsonism only at a medical facility outside the system. In addition, the Olmsted County population is stable, especially for subjects 65 years or older. Finally, the agreement of autopsy findings with the clinical diagnosis of proteinopathy was high, suggesting that a clinical classification of patients with parkinsonism in synucleinopathies and tauopathies is valid.

Our study also has a number of limitations. First, some of the subjects with parkinsonism may have been unaware of their symptoms and may not have received a diagnosis within the incidence period. However, our data collection spanned 20 years, and we collected data for an additional 5 years after the incidence period (2006-2010). This additional collection period allowed us to retrodate the time of onset of symptoms appropriately when needed. Second, the diagnoses obtained through review of historical medical records may be unreliable. The documents available in the records-linkage system were a combination of paper and electronic medical records from multiple health care professionals and multiple institutions. Most patients with parkinsonism had been seen by a neurologist at least once; however, the clinical findings were recorded as part of routine clinical practice and were not standardized for research (eg, standard research scales for parkinsonism or for dementia were not used). Our small reliability study showed an agreement of 90.0% between the 2 neurologists for parkinsonism. However, the agreement by type of parkinsonism was less complete (74.1%). Third, because neurologic practices and diagnostic criteria changed over time, some patients had more complete diagnostic information available in their records than others. In fact, the discordant diagnoses observed in our reliability study involved patients with

<table>
<thead>
<tr>
<th>Type of parkinsonism</th>
<th>Lewy Bodies</th>
<th>Tau</th>
<th>Other*</th>
<th>Total</th>
<th>Agreement, No. (%)</th>
</tr>
</thead>
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<tr>
<td>Parkinson disease</td>
<td>17</td>
<td>1</td>
<td>2</td>
<td>20</td>
<td>17/20 (85.0)</td>
</tr>
<tr>
<td>Parkinsonism with dementia</td>
<td>24</td>
<td>1</td>
<td>6</td>
<td>31</td>
<td>24/31 (77.4)</td>
</tr>
<tr>
<td>Multiple system atrophy</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>4/5 (80.0)</td>
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<tr>
<td>Corticobasal syndrome</td>
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<td>2</td>
<td>0</td>
<td>2</td>
<td>2/2 (100.0)</td>
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<tr>
<td>Drug-induced parkinsonism</td>
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<td>0</td>
<td>3</td>
<td>4</td>
<td>3/4 (75.0)</td>
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<td>Vascular parkinsonism</td>
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<td>0</td>
<td>1</td>
<td>1</td>
<td>1/1 (100.0)</td>
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<tr>
<td>Parkinsonism unspecified</td>
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<tr>
<td>Total</td>
<td>46</td>
<td>5</td>
<td>14</td>
<td>65</td>
<td>53/65 (81.5)</td>
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<table>
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<th>Proteinopathy</th>
<th>Lewy Bodies</th>
<th>Tau</th>
<th>Other*</th>
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<th>Agreement, No. (%)</th>
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<tr>
<td>Synucleinopathy</td>
<td>45</td>
<td>3</td>
<td>8</td>
<td>56</td>
<td>45/56 (80.4)</td>
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<tr>
<td>Tauopathy</td>
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<td>0</td>
<td>2</td>
<td>2/2 (100.0)</td>
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<tr>
<td>Other parkinsonism</td>
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<td>0</td>
<td>6</td>
<td>7</td>
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<tr>
<td>Total</td>
<td>46</td>
<td>5</td>
<td>14</td>
<td>65</td>
<td>53/65 (81.5)</td>
</tr>
</tbody>
</table>

* Neuropathological findings listed as "other" include Alzheimer disease pathologies.
* Synucleinopathies include Parkinson disease, parkinsonism with dementia, and multiple system atrophy. Tauopathies include corticobasal syndrome. Other parkinsonism includes drug-induced parkinsonism, vascular parkinsonism, and parkinsonism unspecified.
* Six of these 8 cases had incontinence of substantia nigra without evidence of Lewy body or tau pathology.

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multiple and atypical parkinsonian features. The classification of patients in a single clinical type involved clinical judgment (eg, parkinsonism with concurrent use of neuroleptics, autonomic dysfunction, and cognitive disorders). The adjudication of all patients by a single movement disorders specialist should have attenuated these possible differences; however, 15.5% of the patients with parkinsonism remained unspecified.

Fourth, the clinical diagnosis might not have corresponded with pathological findings in some cases. The agreement between clinically presumed proteinopathy and autopsy was 81.5% in our population-based sample. Clinico-pathological concordance of greater than 90% has been described when cases were selected using strict clinical criteria. On the other hand, a patient may have more than 1 pathological finding at autopsy; thus, the clinical diagnosis of a single presumed proteinopathy may be incomplete. None of the brains exhibited comorbid Lewy body pathology and tau pathology in our study. Fifth, we found only 20 patients with a presumed tauopathy manifesting with parkinsonism. Therefore, the results for tauopathy and its subtypes should be interpreted cautiously.

In conclusion, our study provides new data on the incidence of clinically presumed proteinopathies related to parkinsonism in men and women. Synucleinopathies are the most common type of proteinopathies; among them, PD is the most common subtype, followed by parkinsonism with dementia and MSA. Tauopathies manifesting with parkinsonism are rare disorders, and PSP is more common than CBS. The incidence of proteinopathies increases with age, and most types of proteinopathies occur more frequently in men than women.


