Movement Disorders
Vol. 21, No. 9, 2006, pp. 1343–1349

Subtypes of Mild Cognitive Impairment in Parkinson's Disease: Progression to Dementia

Carmen Cristea Janvin, M Psych,[1] Jan Petter Larsen, MD, PhD,[2] Dag Aarsland, MD, PhD,[1]* and Kenneth Hugdahl, M Psych, PhD[3]

[1]*Stavanger University Hospital, Section of Geriatric Psychiatry, Stavanger, Norway*
[2]*Stavanger University Hospital, Department of Neurology, Stavanger, Norway*
[3]*University of Bergen, Department of Biological and Medical Psychology, Bergen, Norway*

Abstract: The aim of this study was to establish the rate of progression from mild cognitive impairment (MCI) to dementia in patients with Parkinson's disease (PD). PD patients without dementia were recruited in 1997 from an ongoing prospective epidemiological study. The assessment included neurological and psychiatric examinations, a clinical interview based on the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R) criteria for dementia, and a battery of neuropsychological tests. PD was diagnosed according to established criteria, dementia was diagnosed according to the DSM-III-R criteria, and subtypes of MCI were classified according to modified Petersen's criteria. Seventy-two nondemented PD patients were included. A total of 34 were cognitively intact, whereas 38 were diagnosed with MCI (amnestic, n = 6; single nonmemory domain, n = 17; multiple domains slightly impaired, n = 15). Fifty-nine patients (82%) completed follow-up examination 4 years later, and 18 (62%) of the patients with MCI and 6 (20%) of the cognitively intact PD patients were demented ($P = 0.001$). Single domain nonmemory MCI and multiple domains slightly impaired MCI were associated with later development of dementia ($P = 0.003$; $P = 0.04$), whereas amnestic MCI subtype was not ($P = 0.76$). We conclude that patients with PD and MCI had a higher risk of developing dementia than cognitively intact PD patients, suggesting that MCI in PD is an early manifestation of dementia. However, these findings should be interpreted with caution due to the relatively small number of subjects included in this study. © 2006 Movement Disorder Society

Key words: Parkinson's disease; mild cognitive impairment; dementia

Parkinson's disease (PD) is often associated with mild cognitive impairment and dementia. The point-prevalence of dementia is 31.5%,[1] and patients with PD have an almost sixfold increased risk of developing dementia compared to healthy controls.[2] In addition, cognitive impairment is common even in nondemented patients with PD.[3,4] Among the few prospective studies reported, impairments on tests of executive functioning and memory have been found to predict subsequent dementia in PD.[5,6] However, these associations are based on group mean scores and, thus, may be of limited value in assessing the risk of developing dementia in an individual patient. Because up to 80%[7] of patients with PD will ultimately develop dementia, such information would be of key importance for planning patient management, because cognitive impairment in PD affects quality of life,[8] contributes to caregiver distress,[9] and has been associated with nursing home placement.[10] In addition, it would provide important background information for future prevention trials of dementia in PD.

The concept mild cognitive impairment (MCI) has been introduced, and a considerable proportion of elderly subjects can be classified as having MCI.[11] Subjects with MCI have an increased risk of dementia, with an annual progression to dementia between 6% and 15%.[12] Recently, the MCI subtypes amnestic, single domain nonmemory, and global MCI were described.[13] There is some evidence suggesting that the different MCI subtypes progress to different dementia disorders.[14] Patients with amnestic MCI usually progress to Alzheimer's dis-

*Correspondence to: Dr. Dag Aarsland, Stavanger University Hospital, Department for Geriatric Psychiatry, PO Box 1163 Hillevaag, 4004 Stavanger, Norway. E-mail: daa@sir.no

Received 4 July 2005; Revised 13 January 2006; Accepted 15 January 2006

Published online 23 May 2006 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.20974

ease (AD) at a high rate,[12] whereas patients with single nonmemory MCI (i.e., executive or visuospatial impairment) are more likely to progress to a non-AD dementia such as dementia with Lewy bodies,[15] frontotemporal dementia, vascular dementia, or primary progressive aphasia.[14] However, the diagnostic criteria for MCI have not been validated for PD populations.

Different cognitive profiles may exist within PD. In a study of recently diagnosed patients with PD,[4] 11% had a specific frontostriatal type deficit, 8% had a specific temporal lobe type deficit, whereas 18% had cognitive deficits in both domains. In a community-based study of PD patients with longstanding disease, over 50% of the nondemented patients with PD had some form of cognitive impairment: 20% exhibited predominantly memory deficits, 30% a dominant executive impairment, whereas 50% had a global cognitive impairment.[3] The importance of different cognitive profiles for the development of subsequent dementia in patients with PD is not known.

The aim of this study was to investigate whether MCI is associated with development of dementia in patients with PD. Furthermore, we wanted to examine the existence of different subtypes of MCI in these patients, and their influence on the rate of developing dementia.

SUBJECTS AND METHODS

Subjects

One hundred forty-five patients with PD from an ongoing prospective, community-based study of PD in the county of Rogaland, Norway[16] were invited during 1996/1997 to participate in the baseline evaluation of the present study. They completed a comprehensive assessment consisting of neurological, psychiatric, and neuropsychological evaluations. They were re-assessed 4 years later with the same evaluations as performed at baseline.

A group of healthy elderly controls with similar age, education, and sex distribution as the patients with PD performed the same cognitive test battery at baseline to obtain normative data. They were either relatives of the patients or relatives of inpatients in the psychogeriatric ward at the Stavanger University Hospital. None had a history of alcoholism, drug abuse, psychiatric illness, central nervous system disease, or head injury, and none were currently taking centrally active drugs. Individuals with evidence of intellectual deterioration (Mini-Mental State Examination [MMSE] score < 25) were not included.

Independent raters who were blind to the diagnostic and motor evaluations performed the neuropsychiatric and neuropsychological assessments. The study was approved by the Regional Ethics Committee for Medical Research at the University of Bergen, and all subjects provided written informed consent.

Diagnosis and Clinical Evaluation of PD

Information on disease history was obtained in a semi-structured interview conducted by a neurologist. A diagnosis of PD required the presence of at least two of the four cardinal symptoms of PD and at least a moderate response to levodopa. Patients with clinically significant cognitive impairment at disease onset, other neurologic diagnoses, or drugs that could cause parkinsonism or the presence of radiologic structural brain abnormalities compatible with diagnoses other than PD were excluded.[17] PD was staged using the Hoehn & Yahr scale.[18] The diagnostic evaluation was performed at each evaluation, and only those patients who fulfilled the diagnostic criteria for PD at each examination were included. None of the patients with PD used either anticholinergic parkinsonian medication or cholinesterase inhibitors. Autopsy has been performed in a subgroup of 22 patients of this cohort, and in all cases, the neuropathological diagnosis was consistent with PD.[19]

Assessment of Cognition

Patients and control subjects were given a neuropsychological battery consisting of the following tests: (1) The multiple choice version of the Benton Visual Retention Test (BVRT), designed to assess short-time visual memory: subjects recognize one or more designs that they have seen before.[20] (2) The Judgment of Line Orientation test (JLO), designed to assess visuospatial abilities: subjects estimate angular relationship between line segments by visually matching angled line pairs to 11 numbered radii forming a semicircle.[21] (3) The Stroop Word Test (SWT),[22] designed to assess selective attention/executive functions. Subjects name the colors of colored patches (first card), read printed words (second card), and read printed color names in which the ink used for printing is a color different from the color designed by the printed name (third card). These neuropsychological tests were selected to identify cognitive deficits typically occurring in PD[23] and were as much as possible independent of motor abilities. The tests were administered by a neuropsychologist, and scored according to conventional procedures outlined in the test manuals. In addition, two cognitive screening instruments, the MMSE[24] and the Dementia Rating Scale (DRS)[25] were administered. Severity of depression was measured using Beck Depression Inventory (BDI).[26]

Diagnosis of Dementia

The diagnosis of dementia according to the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R) was made by 2 of the authors (D.A. and J.P.L.) based on an interview administered by an experienced clinician to a caregiver using the DSM-III-R[27] dementia criteria as a guide, and the performance on the cognitive rating scales. Population-based, age- and education-corrected normative data for the MMSE[28] and DRS[29] were used, and scores below the lowest quartile (MMSE) or below 19th percentile (DRS) were considered as cognitive impairment. In cases of inconsistencies between these measures, all the available material was reviewed, and both raters made a diagnosis of dementia or not independently according to the DSM-III-R criteria for dementia. In cases of disagreement, a consensus diagnosis was made.

Diagnosis of MCI

A diagnosis of MCI was made according to a modified version of the criteria proposed by Petersen and colleagues[13]: MCI was defined as impaired performance (i.e., 1.5 standard deviation or more below the mean of the control group) on one, two, or all three neuropsychological tests. In addition, information regarding memory complaint or other subjective cognitive deficits was gathered by means of the caregiver-based interview and the mentation item from the Mental subscale of the Unified Parkinson's Disease Rating Scale.[30] Cognitive impairment should not be severe enough to affect activities of daily living; thus, the criteria for dementia were not met. Three subtypes of cognitive impairment were identified: (1) amnestic MCI, i.e., individuals with impaired performance on the BVRT but who are performing reasonably well on the other neuropsychological tests; (2) multiple domains slightly impaired MCI, i.e., impairment on two or more cognitive tests, without requiring memory deficit; (3) single nonmemory domain MCI, i.e., impairment in a single cognitive domain other than memory, on JLO or SWT.

Statistics

Comparisons between groups for normally distributed continuous data were made using Student's *t* test and one-way analysis of variance. Categorical data were analyzed by using the χ^2 test. Type of MCI at baseline were entered in a binary logistic regression model together with factors possibly associated with incident dementia (i.e., age, sex, education, and Hoehn & Yahr stage), with the dementia diagnosis as the dependent variable. The forward stepping method was used. The *P* value for entering a variable was 0.05 and for removing a variable was 0.10. All analyses were computed using SPSS version 12.0.1 statistical software.

TABLE 1. *Demographic and clinical characteristics of PD patients without dementia and control subjects*[a]

Variables	Nondemented PD (n = 72)	Control subjects (n = 38)	*P* values
Sex M/F	32/40	11/27	
Education, years	9.6 (3.4)	9.8 (3.3)	0.77
Age, years	71.0 (8.1)	68.7 (9.4)	0.19
MMSE score	28.7 (1.8)	29.0 (1.1)	0.40
DRS total score	139.4 (5.1)	141.3 (3.6)	0.04
BVRT score	10.5 (2.3)	11.6 (1.8)	0.01
JLO score	21.0 (5.1)	23.2 (4.1)	0.02
SWT, time, seconds	101.8 (46.0)	79.2 (25.2)	0.007

[a]Values are mean (SD). The *P* values are from Student's *t* test and χ^2 test.

PD, Parkinson's disease; MMSE, Mini-Mental State Examination; DRS, Dementia Rating Scale; BVRT, Benton Visual Retention Test; JLO, Judgment of Line Orientation test; SWT, Stroop Word Test.

RESULTS

Baseline Assessment

There were 11 patients who declined to participate, 58 (43.3%) of the remaining 134 patients with PD had dementia, and 76 (56.7%) were without dementia, but 4 of these did not perform all the neuropsychological tests. Thus, 72 nondemented PD patients comprised the at-risk population. The control group had similar demographic characteristics and MMSE scores as the nondemented PD patients (Table 1), but performed better on all the neuropsychological tests. Of the nondemented PD patients, 34 PD patients (47.2%) were cognitively intact, whereas 38 (52.8%) were diagnosed with MCI. Twenty-six (68%) cognitively impaired PD patients also reported memory complaint or other subjective cognitive impairment. The following MCI subtypes were identified: amnestic type (n = 6; 15.8%), single nonmemory domain type (n = 17, 44.7%), and multiple domains slightly impaired type (n = 15; 39.5%). The demographic and clinical characteristics of these subgroups are shown in Table 2.

Among the patients with single nonmemory domain MCI, 10 patients had an executive impairment (i.e., impaired SWT), whereas the remaining 7 patients had a visuospatial impairment (i.e., impaired JLO). Within the group of patients with multiple domains slightly impaired MCI, 1 patient had executive and visuospatial impairment, 6 had executive and memory impairment, 4 had memory as well as visuospatial impairment, and the remaining 4 patients had impaired performance on all three neuropsychological tests.

TABLE 2. *Baseline characteristics of patients with MCI-PD and cognitively intact PD patients*[a]

Variables	MCI amnestic (n = 6)	MCI single domain nonmemory (n = 17)	MCI multiple domains slightly impaired (n = 15)	Cognitively intact (n = 34)
Gender M/F	3/3	8/9	7/8	14/20
Education, years	8.4 (2.1)	9.6 (2.4)	8.5 (3.5)	10.2 (3.9)
Age, years	71.5 (5.7)	73.4 (6.9)	74.8 (5.4)*	68.1 (9.2)
Disease duration, years	10.6 (4.0)	11.4 (4.4)	11.6 (4.7)	12.2 (4.6)
Age at onset, years	60.2 (6.9)	62.2 (8.1)	62.8 (7.9)	56.0 (11.7)
Hoehn & Yahr stage	2.2 (0.4)	2.6 (0.5)	3.3 (0.1)**#	2.3 (0.6)
BDI score	12.0 (9.6)	11.5 (6.2)	13.0 (6.8)	8.7 (6.0)
MMSE score	29.0 (1.5)	28.7 (1.9)	27.3 (2.1)	29.2 (1.5)
DRS total score	140.8 (4.0)	140.2 (4.2)	134.1 (6.0)**¤¤#	140.9 (4.0)
BVRT score	7.8 (1.1)	11.4 (0.8)##	7.4 (1.7)**¤¤	11.9 (1.5)
JLO	20.1 (1.9)	18.7 (5.4)**	16.7 (4.2)**	24.0 (3.8)
SWT, time seconds	73.6 (24.1)	123.9 (39.9)#**	146.6 (56.1)##**	76.0 (19.3)

[a]Values are mean (SD). The *P* values are from one-way analyses of variance comparing the groups. Different from cognitive intact patients: $*P < 0.05$, $**P < 0.001$. Different from the amnestic MCI group: $\#P < 0.05$, $\#\#P < 0.001$. Different from the single domain nonmemory MCI group: $¤P < 0.05$, $¤¤P < 0.001$.

MCI, mild cognitive impairment; PD, Parkinson's disease; BDI, Beck Depression Inventory; MMSE, Mini-Mental State Examination; DRS, Dementia Rating Scale; BVRT, Benton Visual Retention Test; JLO, Judgment of Line Orientation; SWT, Stroop Word Test.

Follow-Up Assessment

Twenty-nine (76%) of the patients with MCI (2 patients with amnestic MCI, 7 with multiple domains slightly impaired type MCI, and 9 with single nonmemory domain MCI) and 30 (88%) of the cognitively intact patients completed follow-up assessment (10 patients had died and 3 declined to participate further). A total of 18 (62%) of the patients with MCI were demented at follow-up, compared to only 6 (20%) of the cognitively intact PD patients ($\chi^2 = 10.81$; df = 1; $P = 0.001$). There were 7 (63%) of the patients with multiple domains slightly impaired type and 9 (69%) of the patients with single nonmemory domain impairment type who had developed dementia at follow-up, compared to 2 (40%) of the patients with amnestic type MCI (Fig. 1). The difference between the three subgroups with regard to the proportion of PD patients developing dementia was not statistically significant (χ^2 test = 1.32; df = 2; $P = 0.51$). There were no statistically significant differences between the MCI patients who became demented or not with regard to baseline demographic and clinical variables, except that MCI-PD patients who became demented had higher baseline scores on the BDI (Table 3).

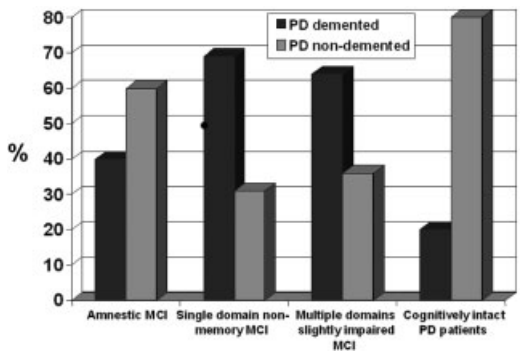

FIG. 1. Dementia status at follow-up according to cognitive status at baseline. PD, Parkinson's disease; MCI, mild cognitive impairment.

Logistic regression was used to identify whether MCI and MCI subtypes were significantly associated with incident dementia in multivariate analyses controlling for age, sex, education, and Hoehn & Yahr stage. MCI at baseline was strongly associated with later development of dementia ($P = 0.006$; odds ratio [OR], 4.8; 95% confidence interval [CI], 1.58–14.8). The significant effect on dementia in MCI was evident even after controlling for the BDI scores at baseline ($P = 0.01$; OR, 4.2; 95% CI, 1.3–13.3). The initial regression model with age, sex, education, and Hoehn & Yahr stage as covariates was repeated to identify whether the subtype of MCI at baseline (i.e. amnestic, single domain nonmemory, and multiple domains slightly impaired) was associated with the development of dementia. Single domain nonmemory MCI ($P = 0.003$; OR, 12.9; 95% CI, 2.44–68.97) and multiple domains slightly impaired MCI ($P = 0.04$; OR, 5.8; 95% CI, 1.04–33.223) were associated with later development of dementia, but not amnestic MCI ($P = 0.76$; OR, 1.41; 95% CI, 0.11–19.05).

After a detailed search through the medical records of the 13 patients who did not participate at follow-up, we were able to establish the dementia status for 9 of these patients: 3 patients became demented, whereas 6 patients did not. For 2 patients, there was no information available, 1 died 1 month after the baseline interview, and 1 had a severe cerebrovascular incident. When all 68 sub-

TABLE 3. *Baseline demographic and clinical characteristics of MCI-PD patients with or without incident dementia*[a]

Variables	PD who became demented (n = 18)	PD who did not become demented (n = 11)	*P* value
Age, years	73.4 (6.3)	73.9 (6.9)	0.85
Sex M/F	10/8	4/7	0.31
Education, years	8.5 (2.8)	8.9 (2.9)	0.71
Age at onset, years	61.7 (7.9)	62.0 (7.5)	0.92
Disease duration, years	12.0 (4.4)	10.8 (4.0)	0.48
Hoehn & Yahr stage	2.9 (0.6)	2.7 (0.1)	0.52
MMSE, score	27.8 (2.4)	29.1 (1.0)	0.09
DRS total, score	138.0 (5.0)	138.3 (6.9)	0.89
BVRT, score	9.5 (2.3)	9.5 (1.9)	0.95
JLO, score	17.5 (4.5)	18.5 (4.7)	0.57
SWT time, seconds	127.6 (45.8)	108.9 (37.1)	0.26
BDI, score	14.2 (5.1)	8.3 (7.3)	0.02

[a]Values are mean (SD). The *P* values are from Student's *t* tests and χ^2 tests.

MCI, mild cognitive impairment; PD, Parkinson's disease; MMSE, Mini-Mental State Examination; DRS, Dementia Rating Scale; BVRT, Benton Visual Retention Test; JLO, Judgment of Line Orientation; SWT, Stroop Word Test; BDI, Beck Depression Inventory.

jects with information on dementia status were included, the difference in dementia among cognitive intact and MCI patients was still highly statistically significant ($\chi^2 = 10.38$; df = 1; $P = 0.001$). The difference between the three MCI subgroups with regard to the proportion of PD patients developing dementia remained not statistically significant ($\chi^2 = 2.54$; df = 2; $P = 0.28$). In the regression analyses, MCI at baseline was still associated with later development of dementia ($P = 0.005$; OR, 5.1; 95% CI, 1.51–16.24). Single domain nonmemory MCI ($P = 0.006$; OR, 8.3; 95% CI, 1.8–37.5) remained associated with later development of dementia, but not amnestic MCI ($P = 0.7$; OR, 1.6; 95% CI, 0.16–19.03) or multiple domains slightly impaired MCI ($P = 0.46$; OR, 1.8; 95% CI, 0.34–10.42).

DISCUSSION

The main finding of this study was that 62% of the patients with MCI-PD developed dementia during the 4-year period between baseline and follow-up assessments compared to only 20% of the cognitively intact patients with PD. This is a novel finding, showing that the conversion rate of MCI to dementia is at least as high as in non-PD individuals with MCI in the general population. Thus, our results suggest that MCI is not a stable condition in PD but, rather, represents the initial stage of a progressive cognitive decline leading to dementia.

These findings support and extend the results from previous longitudinal studies showing that impairments on selected neuropsychological tests are associated with later dementia.[5,6] Furthermore, although the mean rate of cognitive decline in PD is stable over time, there is considerable interindividual variation in the rate of cognitive decline.[31] Thus, the presence of MCI seems to be a key factor in identifying patients with a high risk of developing dementia.

We identified subtypes of MCI and their conversion rate to dementia. The majority of patients with MCI had nonmemory subtypes, that is, single domain nonmemory and multiple domains slightly impaired MCI. These subtypes were associated with later development of dementia. Although the proportion of patients with PD and amnestic type MCI who progressed to dementia was twice that of the cognitively intact patients, the difference did not reach statistical significance. The small number of subjects with amnestic MCI in our sample, resulting in a low statistical power, precludes any firm conclusions regarding whether the different MCI subtypes have different risk of developing dementia.

Depression is associated with cognitive impairments in subjects with[32] and without PD.[33] In this study, MCI-PD patients who developed dementia had higher BDI depression scores than those who did not. Thus, the progression of cognitive decline may be secondary to depression. However, the multivariable analysis showed that MCI was associated with incident dementia even after controlling for depression, and depression was not an independent risk factor for dementia. Similar findings have been reported in most previous prospective studies using multivariable analysis.[2,34] Thus, although depression clearly affects cognition in PD, it is unlikely that the relationship between MCI and incident dementia can be explained by depression.

One of the strengths of this study was the recruitment of subjects from a community-based cohort of patients

with PD without dementia who had been followed up for 4 years before inclusion and assessed with a comprehensive battery of neurological, neuropsychiatric, and cognitive rating scales.[2] Second, the diagnosis of PD was consistently made at neurological examinations by the same study group at three consecutive assessments and was confirmed by autopsy in 22 cases. High diagnostic accuracy, up to 90%, can be achieved in expert groups,[35] especially in patients assessed by the same neurologist in long-term clinical trials using accepted clinical criteria.[36] Third, the long follow-up time allowed us to detect cognitive changes in PD patients that would have not been detected by shorter follow-up times. The attrition rate was low (18%), and it was mainly due to death. Explicit and standardized criteria for dementia, MCI, and PD were used, and the assessment of dementia was performed blind to the motor evaluation. Finally, tests were chosen that were independent of motor functioning and were focused on cognitive domains known to be affected in PD, such as executive, visuospatial, and memory functions.

As most clinical studies, the current study has also some limitations that should be addressed. The sample of PD patients did not include patients with early PD, and our results, therefore, may not be representative for early PD. Each subgroup of MCI-PD patients included a small number of patients each, resulting in low statistical power to detect differences between MCI subtypes. Studies including larger numbers of patients are needed to further explore the relationship between the type of MCI and the risk for developing later dementia. The relatively high drop out rate due to the long test–retest interval might influence the results. However, when the 9 additional patients were included in the analyses, the results did not change significantly. The neuropsychological battery was rather brief; thus, the full spectrum of cognitive impairment in PD may not have been covered. Non-PD patients were not included; therefore, firm conclusion regarding the rate of progression from MCI to dementia in PD relative to the rate in non-PD subjects cannot be made. Finally, with the long interval between baseline and follow-up, a substantial proportion of patients were lost due to death. Because mortality in PD is associated with cognitive impairment,[37] the attrition may not be random and, thus, may lead to an underestimate of the conversion rate of dementia in the MCI group.

In summary, our results indicate that the presence of MCI is associated with subsequent dementia in patients with PD. However, the results should be interpreted with caution due to the relative number of patients with MCI. Dementia is a key determinant of quality of life of patients and caregivers, nursing home admission, and mortality in PD. Thus, our findings have implications for patient management. Patients with PD should be regularly assessed with neuropsychological assessment. Even brief test batteries may identify patients at high risk for dementia, and these patients should be carefully monitored for progression to dementia. Treatment is now available for PD with dementia,[38] and future studies should explore whether the progression from MCI to dementia in PD can be reduced.

Acknowledgments: Thanks go to Drs. Elise Tandberg, Ernst G. Nessler, Guido Alves, and Michaela Gjerstad of the Department of Neurology, Stavanger University Hospital, Stavanger, Norway, for contributing to data collection; to Prof Robert Perry, Newcastle General Hospital, Newcastle, United Kingdom, for performing neuropathological assessment; to statistician Jan Terje Kvaloy, University of Stavanger, Norway, for statistical assistance; and to Prof Clive Ballard, Institute of Psychiatry, King's College, London, UK, for expert comments on a previous draft.

REFERENCES

1. Aarsland D, Zaccai J, Brayne C. A systematic review of prevalence studies of dementia in Parkinson's disease. Mov Disord 2005;20:1255–1263.
2. Aarsland D, Andersen K, Larsen JP, et al. Risk of dementia in Parkinson's disease: a community-based, prospective study. Neurology 2001;56:730–736.
3. Janvin C, Aarsland D, Larsen JP, Hugdahl K. Neuropsychological profile of patients with Parkinson's disease without dementia. Dement Geriatr Cogn Disord 2003;15:126–131.
4. Foltynie T, Brayne CE, Robbins TW, Barker RA. The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study. Brain 2004;127(Pt 3):550–560.
5. Levy G, Jacobs DM, Tang MX, et al. Memory and executive function impairment predict dementia in Parkinson's disease. Mov Disord 2002;17:1221–1226.
6. Woods SP, Troster AI. Prodromal frontal/executive dysfunction predicts incident dementia in Parkinson's disease. J Int Neuropsychol Soc 2003;9:17–24.
7. Aarsland D, Andersen K, Larsen JP, Lolk A, Kragh-Sorensen P. Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. Arch Neurol 2003;60:387–392.
8. Schrag A, Jahanshahi M, Quinn N. What contributes to quality of life in patients with Parkinson's disease? J Neurol Neurosurg Psychiatry 2000;69:308–312.
9. Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. Int J Geriatr Psychiatry 1999;14:866–874.
10. Aarsland D, Larsen JP, Tandberg E, Laake K. Predictors of nursing home placement in Parkinson's disease: a population-based, prospective study. J Am Geriatr Soc 2000;48:938–942.
11. Graham JE, Rockwood K, Beattie BL, et al. Prevalence and severity of cognitive impairment with and without dementia in an elderly population. Lancet 1997;349:1793–1796.
12. Petersen RC, Smith GE, Waring SC, et al. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;56:303–308.
13. Petersen RC, Doody R, Kurz A, et al. Current concepts in mild cognitive impairment. Arch Neurol 2001;58:1985–1992.
14. Petersen RC. Mild cognitive impairment as a diagnostic entity. J Intern Med 2004;256:183–194.

15. Boeve BF, Ferman TJ, Smith GE, et al. Mild cognitive impairment preceding dementia with Lewy bodies [abstract]. Neurology 2004; 62;A29S.
16. Tandberg E, Larsen JP, Nessler EG, Riise T, Aarli JA. The epidemiology of Parkinson's disease in the county of Rogaland, Norway. Mov Disord 1995;10:541–549.
17. Larsen JP, Dupont E, Tandberg E. Clinical diagnosis of Parkinson's disease. Proposal of diagnostic subgroups classified at different levels of confidence. Acta Neurol Scand 1994;89:242–251.
18. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967;17:427–442.
19. Aarsland D, Perry R, Brown A, Larsen JP, Ballard C. Neuropathology of dementia in Parkinson's disease: a prospective, community-based study. Ann Neurol 2005;58:773–776.
20. Benton AL. The Revised Visual Retention Test. 4th ed. New York: Psychological Corporation; 1974.
21. Benton AL, Varney NR, Hamsher KD. Visuospatial judgment. A clinical test. Arch Neurol 1978;35:364–367.
22. Golden. Stroop Color and Word Test. Chicago: Stoelting; 1978.
23. Dubois B, Pillon B. Cognitive deficits in Parkinson's disease. J Neurol 1997;244:2–8.
24. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
25. Mattis S. Dementia rating scale. In: Bellak L, Karasu TB, editors. Geriatric Psychiatry: A Handbook for Psychiatrists and Primary Care Physicians. New York: Grune and Stratton; 1976. p 108–121.
26. Beck AT. Beck Depression Inventory. San Antonio, TX: Psychological Corporation; 1978.
27. Diagnostic and statistical manual of mental disorders. 3rd, revised ed. Washington, DC: American Psychiatric Association; 1987.
28. Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA 1993;269:2386–2391.
29. Lucas JA, Ivnik RJ, Smith GE, et al. Normative data for the Mattis Dementia Rating Scale. J Clin Exp Neuropsychol 1998;20:536–547.
30. Fahn S, Elton RL. Members of the UPDRS Development Committee. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne DB, Lieberman A, editors. Recent Development in Parkinson's Disease. Florham Park, NJ: Macmillan Health Care Information; 1987. p 153–163.
31. Aarsland D, Andersen K, Larsen JP, et al. The rate of cognitive decline in Parkinson disease. Arch Neurol 2004;61:1906–1911.
32. Troster AI, Stalp LD, Paolo AM, Fields JA, Koller WC. Neuropsychological impairment in Parkinson's disease with and without depression. Arch Neurol 1995;52:1164–1169.
33. Elderkin-Thompson V, Kumar A, Bilker WB, et al. Neuropsychological deficits among patients with late-onset minor and major depression. Arch Clin Neuropsychol 2003;18:529–549.
34. Hughes TA, Ross HF, Musa S, et al. A 10-year study of the incidence of and factors predicting dementia in Parkinson's disease. Neurology 2000;54:1596–1602.
35. Hughes AJ, Daniel SE, Lees AJ. Improved accuracy of clinical diagnosis of Lewy body Parkinson's disease. Neurology 2001;57: 1497–1499.
36. Hurtig HI, Trojanowski JQ, Galvin J, et al. Alpha-synuclein cortical Lewy bodies correlate with dementia in Parkinson's disease. Neurology 2000;54:1916–1921.
37. Levy G, Tang MX, Louis ED, et al. The association of incident dementia with mortality in PD. Neurology 2002;59:1708–1713.
38. Emre M, Aarsland D, Albanese A, et al. Rivastigmine for dementia associated with Parkinson's disease. N Engl J Med 2004;351: 2509–2518.