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WHAT IS THE CLINICAL PREVALENCE OF LEWY BODY DEMENTIA?

SUKHWINDER SHERGILL
Registrar in Psychiatry, University College Hospital, London, UK

ELEANOR MULLAN
Lecturer in Psychiatry, Department of Psychiatry, University College, London Medical School, UK

PENNY D'ATH
Research Psychologist, Princess Alexandra Hospital, Harlow, UK

CORNELIUS KATONA
Professor of Psychiatry of the Elderly, Department of Psychiatry, University College London Medical School, UK

SUMMARY

The reported prevalence of Lewy body dementia (LBD) has varied from 12% to 20% in postmortem series. Such series may not be representative of the dementia population as a whole. We have attempted to determine the prevalence of LBD in patients referred to a district general hospital with a diagnosis of dementia. The case notes of a consecutive series of patients with a clinical diagnosis of dementia referred to the care of two consultants in old age psychiatry over a period of 1 year ($N = 114$) were analysed using a checklist incorporating the items of the criteria proposed by McKeith and by Byrne for the *in vivo* diagnosis of LBD. The analysis was repeated for the subgroup ($N = 76$) fulfilling ICD 10 criteria for Alzheimer's disease. The prevalence of LBD was 26.3% according to McKeith criteria, 7% according to Byrne probable and 16.6% according to Byrne possible criteria. There were, however, considerable disagreements between different criteria. The frequencies of individual clinical features within subjects fulfilling and not fulfilling LBD were reviewed. Logistic regression analysis revealed the main clinical features capable of differentiation between LBD and other dementias were: presence of visual or auditory hallucinations; extrapyramidal features or neuroleptic sensitivity syndrome; fluctuating pattern of clinical features over a long period of time (McKeith criteria); and presence of classical Parkinsonism with simultaneous or earlier onset of dementia (Byrne criteria). The results were essentially similar in the Alzheimer's disease subsample. A significant proportion of patients with dementia referred to an old age psychiatry service thus fulfil *in vivo* criteria for LBD. The variation in frequency of diagnosis of LBD by the different criteria suggests that these clinical criteria may need revising.

KEY WORDS—Lewy body dementia, prevalence, criteria.

F. H. Lewy described inclusion bodies in the basal ganglia of patients with paralysis agitans (Parkinson's disease) (Lewy, 1912). Following recent advances in immunocytochemical techniques (Lowe *et al.*, 1988; Kuzuhara *et al.*, 1988), they have been identified in the cerebral cortex as well as in the basal ganglia. Lewy bodies in the cortex have been found in association with dementia (with and without the characteristic neuropathological features of Alzheimer's disease) in patients who did not have a primary diagnosis of Parkinson's disease. Such 'Lewy body disease' (LBD) has recently come to be recognized as an important type of dementia. Its reported prevalence in postmortem series of elderly patients with dementia has varied from 12 to 20% (Table 1).

Retrospective case note analysis of neuropathologically defined cases has suggested that some clinical features occur more frequently in demented patients with cortical Lewy bodies than in those in whom cortical Lewy bodies were not found. For example, an increased sensitivity to neuroleptics has been reported in the neuropathologically

Address for correspondence: Cornelius Katona, MD, FRCPsych, Department of Psychiatry, UCLMS, Wolfson Building, Middlesex Site, London W1N 8AA, UK. Tel: 071–380–9475. Fax: 071–323–1459.

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Table 1

Investigators	Year	LBD	Nature	Sample size	Comments
Forno and Langston	1988	5%	PM	260	Consecutive autopsies; % dementia not known
Byrne *et al.*	1989	7%	PM (total)	216	Referrals for postmortem over 1 year
		27%	PM (dementia)	55	
Joachim *et al.*	1988	18%	PM	150	Clinical diagnosis of Alzheimer's dementia
Dickson *et al.*	1989	13%	PM	216	Degenerative brain disease for evaluation; 3-year period
Perry *et al.*	1990	22%	PM	93	Dementia; age > 70 yr; 5-year period
Hansen *et al.*	1990	36%	PM	36	Alzheimer's disease diagnostic criteria; Parkinsonism excluded

PM, postmortem.

defined group of LBD, which appears to be associated with an increased morbidity and mortality and is therefore clinically important (McKeith *et al.*, 1992). Diagnosis in life would allow the natural history of this disease to be ascertained. This would be useful for clarifying the prognosis of LBD and for assessing the value of therapeutic interventions. Equally important, such identification would prevent the contamination of clinical trials involving patients thought to have a diagnosis of 'pure' Alzheimer's disease. Operational criteria have been proposed by McKeith *et al.* (1992) and by Byrne *et al.* (1991) summarizing these essential clinical features. Byrne's group have further distinguished between 'probable' and 'possible' LBD. Validation of the clinical criteria for LBD depends ultimately on autopsy data (eg McKeith *et al.*, 1994). Postmortem series may, however, not be epidemiologically representative (Brayne, 1993) or even be a true reflection of the patients seen within a clinical service.

This study uses the criteria of McKeith *et al.* (1992) and of Byrne *et al.* (1991) to estimate the prevalence of LBD in a population of patients presenting to the old age service of a district general hospital. It examines whether these criteria define a distinct clinical group of patients and whether similar prevalence rates are apparent in a clinical sample to those found in postmortem studies. In addition, the study examines which individual features within the clinical criteria appear most informative in making a clinical diagnosis of LBD.

SUBJECTS AND METHODS

All cases with a clinical diagnosis of dementia under the care of two consultants in old age psychiatry seen in the year ending September 1992 were identified on the basis of case note review. Clinical diagnoses of Alzheimer's disease and of vascular, alcoholic and mixed dementia were made using ICD 10 criteria. The case notes were further analysed using a checklist (Appendix), which is a summation of the criteria proposed by McKeith *et al.* (1992) and Byrne *et al.* (1991) for *in vivo* diagnosis of LBD.

Using these criteria, patients were divided into the following groups:

1. Patients fulfilling McKeith *et al.* criteria for LBD
2. Patients fulfilling Byrne *et al.* criteria for probable LBD
3. Patients fulfilling Byrne *et al.* criteria for possible LBD

The three groupings (and the Byrne probable and possible in particular) were not treated as mutually exclusive.

The results were analysed using the SPSS package with chi-square tests (Fisher's exact test where appropriate) and subsequent stepwise logistic regression using SPSSPC+ (1992). Analyses were carried out both on the total sample and on those subjects fulfilling ICD 10 criteria for Alzheimer's disease.

Table 2. ICD 10 diagnoses

CD 10 code	Dementia	Number	%	F:M
F00.1	Alzheimer's disease	76	67.0	1:0.4
F01.0	Vascular	30	26.1	1:1.2
01.1				
01.2				
F00.2	Mixed	4	3.5	
$F1_x.73$	Alcoholic	2	1.7	
F02.3	Parkinson's	1	0.9	
F01.1	Vascular and hydrocephalus	1	0.9	

RESULTS

The frequency of ICD 10 diagnoses is noted in Table 2 with female:male ratio for the most common diagnoses. The prevalence of LBD was 26.3% (30) according to McKeith criteria, 7% (8) according to Byrne 'probable' LBD criteria and 16.7% (19) according to Byrne 'possible' LBD criteria. Concordances between criteria are shown in Table 3. Within this population fulfilling criteria for Alzheimer's disease (76 subjects), 32% fulfilled McKeith criteria, 7.5% fulfilled Byrne probable and 17.5% Byrne possible criteria.

Table 3

	Number	McKeith	Byrne possible
McKeith	30		14
Byrne possible	19	14	
Byrne probable	8	8	6
1 of the above	35		

The frequency of occurrence of individual clinical features within the total sample and in the Alzheimer's disease subgroup and the relationship of these features to the diagnosis of LBD according to McKeith and to Byrne (probable and possible combined) criteria are summarized in Table 4.

Significantly more McKeith positive subjects (76%) than McKeith negative subjects (52%) were female ($p > 0.05$). There was no sex difference between Byrne positive (probable or possible) subjects compared to the remainder of the sample. Byrne positive subjects were significantly younger than non-cases ($p < 0.01$), but there was no difference in age between McKeith positive and negative subjects.

There was significantly more usage of neuroleptics in the population fulfilling McKeith criteria: 56.7% of McKeith positives had been treated with neuroleptics compared to 36.1% of the rest ($p < 0.05$). There were strong associations between caseness on both McKeith and Byrne criteria and Parkinson's disease ($p < 0.001$), absence of a history of CVA ($p < 0.001$) and lack of focal neurological signs ($p < 0.01$). Fluctuating impairment and the presence of hallucinations were associated with LBD according to McKeith criteria only ($p < 0.0001$).

In general, the same clinical features distinguished between LBD cases and non-cases in the Alzheimer's disease subgroup. In this group, the presence of an acute confusional state early in the dementia process was significantly associated with LBD on McKeith criteria ($p < 0.05$). Absence of CVA and a lack of focal neurological signs were less strikingly associated with LBD than in the total sample, probably reflecting the small number of Alzheimer's disease subjects positive for these features.

Using logistic regression analysis, the clinical features discriminating between McKeith criteria and the rest in the total sample were:

1. Presence of visual or auditory hallucinations usually accompanied by paranoid delusions
2. Mild spontaneous extrapyramidal features or neuroleptic sensitivity syndrome
3. Fluctuating pattern of clinical features persisting over a long period (weeks or months), often rapid progress to severe dementia

The above features allowed correct prediction in 96.6% of cases.

Clinical features differentiating between Byrne 'probable' criteria and the rest were:

Table 4. Frequency of individual criteria and correlation with McKeith and Byrne criteria (comparing Alzheimer's subgroup)

Criteria		Freq. (*F*)	McKeith positive	Correlation	Byrne positive	Correlation	Freq. in Alzheimer's sub-group	McKeith positive	Correlation	Byrne positive	Correlation
Male		47	7	$p < 0.05$	7	Non-significant	26	6	Non-significant	6	Non-significant
Female		67	23		14		54	20		10	
Age < 75		23	7	Non-significant	9	$p < 0.001$	17	6	Non-significant	8	$p < 0.005$
75+		91	23		12		63	20		8	
Acute confusional states early in	A	80	17	Non-significant	13	Non-significant	58	15	$p < 0.05$	10	Non-significant
dementia	P	34	13		8		22	11		6	
Classical Parkinson's	A	108	24	$p < 0.001$	15	$p < 0.0001$	76	22	$p < 0.01$	12	$p < 0.01$
disease (PD)	P	6	6		6		4	4		4	
Simultaneous PD	A	112	28	Non-significant	19	$p < 0.05$	78	24	Non-significant	14	$p < 0.05$
and dementia	P	2	2		2		2	2		2	
Absence of CVA	A	34	0	$p < 0.0001$	0	$p < 0.001$	9	0	$p < 0.05$	0	Non-significant
	P	80	30		21		71	26		16	
No focal signs	A	28	0	$p < 0.001$	0	$p < 0.01$	5	0	Non-significant	0	Non-significant
except Parkinsonism	P	86	30		21		75	26		16	
3+ signs of	A	99	17	$p < 0.0001$	7	$p < 0.0001$	67	15	$p < 0.0001$	4	$p < 0.0001$
Parkinsonism	P	15	13		14		13	11		12	
Exclude other causes	A	1	0	Non-significant	0	Non-significant	1	0	Non-significant	0	Non-significant
of dementia	P	113	30		21		79	26		16	
Acute onset	A	58	14	Non-significant	7	Non-significant	49	14	Non-significant	7	Non-significant
± plateaux ± psychiatric											
symptoms	P	56	16		14		31	12		9	
Dementia with late	A	99	21	$p < 0.001$	11	$p < 0.0001$	70	19	$p < 0.05$	8	$p < 0.0001$
Parkinsonism	P	15	9		10		10	7		8	
One or two signs	A	70	13	$p < 0.005$	0	$p < 0.0001$	53	12	$p < 0.01$	0	$p < 0.0001$
of Parkinsonism	P	44	17		21		27	14		16	
Fluctuating	A	31	0	$p < 0.001$	3	Non-significant	22	0	$p < 0.0001$	2	Non-significant
impairment with lucid intervals	P	83	30		18		58	26		14	
Hallucinations	A	89	10	$p < 0.0001$	13	Non-significant	60	10	$p < 0.0001$	11	Non-significant
± delusions	P	25	20		8		20	16		5	
Neuroleptic	A	93	15	$p < 0.0001$	6	$p < 0.0001$	63	13	$p < 0.0001$	4	$p < 0.0001$
sensitivity	P	21	15		15		17	13		12	
Unexplained	A	72	21	Non-significant	12	Non-significant	58	19	Non-significant	11	Non-significant
falls	P	42	9		9		22	7		5	
Chronic fluctuating	A	43	0	$p < 0.0001$	3	$p < 0.05$	33	0	$p < 0.0001$	2	$p < 0.001$
course	P	71	30		18		47	26		14	
Neuroleptic	A	67	13	$p < 0.05$	9	Non-significant	46	10	$p < 0.05$	7	Non-significant
usage	P	47	17		12		34	16		9	
Total present		114	30		21		80	26		16	

1. Classical Parkinson's disease, at onset with later emergence of dementia
2. Simultaneous occurrence of dementia and Parkinsonism

These features allowed 100% positive prediction of cases.

Clinical features differentiating best between Byrne 'possible' criteria and rest were:

1. Three or more of the following; (a) tremor; (b) rigidity; (c) postural change; (d) bradykinesia; (e) gait abnormality
2. One or two of the above list under (1)
3. Absence of history of stroke

These features allowed 100% positive prediction.

When the logistic regression analysis was repeated in the Alzheimer's disease subgroup, the clinical features discriminating for subtypes of LBD were as above, with the exception of Byrne possible criteria, where the most discriminating features were as follows:

1. Dementia with acute onset and rapid course sometimes associated with plateaux and frequently associated with psychiatric symptoms
2. One or two of the following: (a) tremor; (b) rigidity; (c) postural change; (d) bradykinesia; (e) gait abnormality
3. Fluctuating pattern of clinical features persisting over a long period (weeks or months). Often rapid progress to severe dementia

DISCUSSION

It would appear that, particularly on the basis of the criteria proposed by McKeith *et al.* (1992), LBD is present in a significant proportion of patients with dementia referred to old age psychiatry services. We have found prevalence rates very similar to those in the postmortem studies listed in Table 1. Most of our LBD positive subjects were within the Alzheimer's disease subgroup, with a much smaller apparent prevalence in those with vascular dementia. This probably reflects the fact that absence of a history of cerebrovascular accidents and lack of focal neurological signs are favoured in the clinical criteria for LBD. There is an increased prevalence of LBD in females in this study which contrasts with other studies (McKeith *et al.*, 1992; Byrne *et al.*, 1989). This may reflect the fact that most subjects with vascular dementia (who would have strong male preponderance) were excluded.

Not surprisingly, our logistic regression analysis identified clusters of clinical features in line with the descriptions incorporated in the Byrne and McKeith criteria. However, not all the individual criteria discriminated effectively between cases and non-cases according to any of the diagnostic systems we used. The most informative criteria for LBD appear to be related to Parkinsonism, to related neuroleptic sensitivity and to the presence of hallucinations with secondary delusions. Parkinsonism in these patients may be supposed to reflect the presence of Lewy bodies in cytoplasm of neurones in the substantia nigra leading to dopaminergic depletion. It has been suggested that hallucinations are due to an imbalance between cholinergic and monoaminergic systems in the temporal lobe (E. K. Perry *et al.*, 1990). These clinical features therefore probably reflect distinct biological processes. Neuroleptic usage was commoner in subjects fulfilling McKeith criteria for LBD. This may reflect the relatively high prevalence of hallucinations within the LBD group, and is obviously an area of concern in the light of the (more striking) excess of neuroleptic sensitivity in these subjects.

In our series, the Byrne 'probable' criteria were the narrowest, with only eight 'positive' subjects. This diagnostic category may be useful for identifying subjects with late or severe LBD. All Byrne 'probable' cases also fulfilled the McKeith criteria, which are more sensitive, particularly in not requiring Parkinsonian features. In general, however, McKeith's and Byrne's criteria identify different clinical groups: the latter concentrating on the dementia of Parkinson's disease (though also incorporating apparent confusional states) and the former focusing on hallucinations, neuroleptic sensitivity and fluctuating impairment and consciousness. This is in keeping with the recent report by Ballard *et al.* (1993), who found that 14/16 day hospital attenders with idiopathic clouding of consciousness fulfilled McKeith criteria for LBD. These findings may reflect the different populations used by McKeith's group (predominantly old age psychiatry drawn) and Byrne's more mixed group (incorporating neurological, old age medicine and old age psychiatry patients) in defining their clinical criteria.

Our study covers a representative sample of patients presenting to a dementia clinic in the UK. A number of methodological problems can, however, be identified. The criteria specified in the

Appendix are not rigorously defined, and the retrospective analysis method we have used is vulnerable to rater bias and, because of inadequate case note information, may underestimate true prevalence both in terms of caseness and at individual clinical feature level. We have also not formally evaluated interrater reliability for the criteria used, though a recent paper by McKeith *et al.* (1994) has established satisfactory interrater reliability for the McKeith criteria. Our recorded frequencies of individual clinical features as well as of LBD diagnoses are comparable with postmortem studies (Jabeen *et al.*, 1990; Cummings *et al.*, 1987). The ICD 10 frequency of dementia subtypes (and sex ratios within them) is also similar to that of published series (Dickson *et al.*, 1989; R. Perry *et al.*, 1990). This suggests that no gross and systematic bias was in operation.

In conclusion, our study suggests that the criteria of McKeith *et al.* (1992) and those of Byrne (1991) both contain several non-discriminating items and that, more importantly, they do not identify the same patients as having LBD. McKeith (personal communication) has found that in postmortem series, both his and Byrne's criteria have high specificity for autopsy-proven LBD, but the Byrne criteria are much less sensitive. Studies in which *in vivo* criteria are applied prospectively with subsequent postmortem validation are clearly needed in order to enable the clinical diagnosis of LBD to be made with confidence.

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