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Editorial

Lewy Body Dementia – Diagnosis and Treatment

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In the foreword to a volume entitled *Recent Advances in Psychogeriatrics* published in 1992, Tom Arie remarked upon the sudden appearance of Lewy body dementia (LBD) on the clinical scene. A diagnosis not previously found in the long list of causes of dementia was apparently being proclaimed as possibly the second most common cause of dementia in the elderly. There has followed considerable debate as to how this new concept should be handled. Points of uncertainty or disagreement include whether or not precise neuropathological criteria of LBD have been established, and, if so, whether such patients have a distinguishable clinical syndrome. If LBD is identifiable ante-mortem, how should patients and their relatives be advised and what implications are there for management?

At least part of the heterogeneity of opinion about LBD probably derives from the fact that patients may present in approximately equal numbers to old age psychiatry services (cognitive impairment, psychosis and behavioural disturbance), geriatric medicine (acute confusional states, syncope and falls), or neurological services (Parkinsonism). An authority from each of these specialities was therefore asked to write a brief review of the topic from their own particular perspective.

The neurologist

Neocortical Lewy bodies (LB), after escaping detection for years, are now in sharp focus as major contributors to dementia and psychiatric symptoms in the elderly. In several autopsy series of demented patients, LB rank as the second most common type of degenerative pathology, occurring in 15–25% of cases, exceeded only by the senile plaques (SP) and neurofibrillary tangles (NFT) of Alzheimer's disease (AD). This brief review, coloured by the experience of a research centre conducting longitudinal studies in dementia, will highlight the overlap between LBD and AD, as well as those features attributable to LB.

A burgeoning nomenclature has been used to describe patients with LBD, reflecting the diversity of clinical and pathological findings. The term 'diffuse Lewy body disease' (DLBD) was originally coined for demented patients whose brains showed widespread LB, found in the hippocampus, temporal lobe, cingulate and neocortex, in addition to their classic sites in the substantia nigra and other subcortical regions. It was assumed that the diffusely distributed LB accounted for dementia and distinguished DLBD from idiopathic Parkinson's disease (PD), in which LBD were thought to be restricted to subcortical areas. However, recent studies have shown that virtually every PD patient has at least some cortical LB.

What then differentiates LBD patients from non-demented PD patients? One factor is the number of LB, particularly in the cortex, as there is a direct correlation between the density of cortical LB and the severity of dementia assessed close to the time of death. Alternatively, the presence of additional pathology, such as that of AD, may add to the LB burden to produce dementia. To clarify the relationship between LB and cognitive or psychiatric symptoms, more information is needed about the physiological function and anatomical connections of the cortical neurons that are vulnerable to LB formation.

Many patients with cortical LB also show SP and NFT. In the hippocampus, the AD pathology may be fairly severe, accounting for memory dysfunction. However, NFT counts usually are much lower in neocortical areas in LBD than in AD, and some patients with LBD have minimal AD pathology. AD lesions and LB are both associated with old age, and their coincidence may be due to chance alone. It is interesting that LB and NFT share several features: both are cytoskeletal derangements containing neurofilaments or related proteins, which undergo phosphorylation and ubiquitination. These events may occur late in lesion formation, and stronger evidence is required to make a case that similar mechanisms lead to the formation of LB and NFT.

Just as cortical LB may evade casual inspection, so can the clinical picture of LBD be overlooked. Since patients with LBD commonly have AD lesions, clinical features usually overlap with those characteristic of AD, and include the gradual onset of forgetfulness, followed by difficulty with word finding, calculation and other cognitive skills. The age of onset of LBD is similar to that of AD, although

men are affected more often than women. In our experience, the pattern of neuropsychological deficits may help to distinguish LBD from 'pure' AD. When matched with AD patients at a similar stage of dementia, LBD patients show more severe impairment on visuospatial tests such as block design, clock drawing or copying figures, and on tests of 'executive function' and problem solving such as the Wisconsin Card Sorting Test, the Trail-Making test, and on category fluency. These areas of impairment resemble the types of neuropsychological deficits reported in PD patients, and reinforce the argument that LB load is an important cause of dementia in PD. With the progression of dementia, the selectivity of this pattern may be lost. The clinical course may be faster in LBD than in AD; occasionally patients progress to severe dementia or death within a year or two after the onset of dementia.

Psychiatric symptoms are common in LBD, as is the case for AD and for dementia associated with PD. In our experience, depression and delusions have a similar frequency in LBD, vascular dementia and AD. Hallucinations, however, seem to be a hallmark of LBD, occurring in up to 50% of patients, often in the absence of an obvious precipitating illness or metabolic disturbance. This is a higher rate than in AD or other dementias, and may result from cholinergic depletion and LB formation in areas such as the temporal lobe, as the hallucinations are almost always visual, and consist of formed images of people or animals. Some patients show fluctuating levels of cognition or alertness, which may last from hours to days, and resemble delirium or transient cerebral ischaemia.

Extrapyramidal signs occur in over 50% of patients with LBD in the absence of neuroleptic exposure, and are generally milder than those found in PD patients. They include bradykinesia, rigidity, hypophonic speech, masked facies, stooped posture, and a slow and shuffling gait; the resting, 'pill-rolling' tremor, one of the hallmarks of PD, is extremely rare. Parkinsonian findings are not unique to LBD, as they may arise in AD, in other degenerative dementias such as progressive supranuclear palsy, or after treatment with neuroleptic medications. About 10–20% of clinically diagnosed AD patients show extrapyramidal signs at an early or intermediate stage of dementia. These patients have a higher prevalence of psychotic symptoms and a more rapid rate of progression than AD patients without extrapyramidal signs, and most likely have an overlap syndrome with underlying neuropathology of AD and LB. However, not all EPS associated with AD can be explained by LB.

Unfortunately there are no clear guidelines for treating patients with LBD. In fact, advice about medication avoidance may be more germane. The combination of dopaminergic deficits with cholinergic depletion make these patients sensitive to several classes of medications. Neuroleptics may provoke dramatic deterioration of cognitive and motor function, and should be used cautiously if required to control psychotic symptoms or agitation. Drugs with anticholinergic activity may produce mental clouding or delirium. Although dopaminergic medications such as L-dopa, the mainstay of treatment in idiopathic PD, are less often effective in LBD, they warrant a trial. Preliminary reports suggest that cholinergic enhancement with tacrine, a cholinesterase inhibitor approved for the treatment of AD, may improve cognition and possibly psychiatric symptoms in LBD. Now that the clinical syndrome of LBD can be diagnosed with reasonable confidence, systematic studies of treatment are both feasible and desirable.

The geriatrician

The term LBD is confusing, especially to clinicians, and is often used indiscriminately to include senile dementia of Lewy body type (SDLT), DLBD, the Lewy body variant of Alzheimer's disease (LBV), and so on. This is hardly surprising, however, as the literature in this field is itself confusing. As a clinician trying to treat a patient, in the absence of any specific treatment for any of the LB variants, I wonder whether it really matters at the moment as long as one remembers to avoid phenothiazines and related compounds if possible. At a scientific level, however, it is an extremely challenging and interesting debate which one day must be resolved. Should one be a 'lumper' or a 'splitter'? Are LB a distinct entity or do they merely represent the microscopic appearance of the end points of differing pathological processes even if they share certain neurochemical features? Certainly, LB in the cortex differ somewhat from those in the brainstem at a light microscopical level, and also biochemically. It has also been claimed that LB from the brains of people with idiopathic PD are different from those of so-called DLBD, but this requires confirmation. Until some order is introduced into the neuropathological descriptions and this is generally agreed and applied, it will continue to be difficult to identify discrete clinical syndromes that may be associated with a particular neuropathological substrate.

Whether or not there are two separate pathological processes, that is, LBD and AD, either of which can

exist independently or together, one being more advanced than the other in a particular brain, whether they are in fact manifestations of a single disease process or whether both these possibilities exist has in my opinion still to be decided. This is further complicated by the description of a subset of patients with three concomitant pathologies – those of AD, diffuse LB and also localised spongiform change predominantly affecting the medial temporal region in which the disease was not transmissible or associated with accumulation or prion protein (i.e. not Creutzfeldt–Jakob disease, CJD) (Hansen *et al*, 1989). Conceptually it is easiest to accept the presence of a spectrum of LB diseases, one of which, SDLT, appears neuropathologically to be commoner among elderly demented patients, characterised by moderate numbers of cortical LB, at least moderate numbers of SP, but fewer or absent NFT, together with a number of subcortical abnormalities.

Psychiatric and neurological features

There are no specific clinical features that reliably indicate the presence of dementia associated with cortical LB. In some patients the clinical course is indistinguishable from AD until quite late in the disorder, while others with so-called typical features eventually prove to have other conditions. Nevertheless, there is a consensus emerging that a progressive dementing illness with marked fluctuation and hallucinations or extrapyramidal features earlier than is usually noted in AD, should raise the possibility of a LBD, when organic illness has been excluded as a cause of the fluctuating cognitive state and in the absence of evidence to support the diagnosis of vascular dementia (McKeith *et al*, 1992*a*). However, these features are not always present in our experience, or that of others (e.g. Förstl *et al*, 1993), although early rigidity is frequently found.

It has also been suggested that such patients show background slowing on their electroencephalogram (EEG), associated with burst patterns that are often frontally dominant at an early stage in the disease compared with the normal EEG or the mild abnormalities observed in early AD (Crystal *et al*, 1990). The pattern of cognitive impairment has been said to affect visuospatial function, attention and verbal fluency more than is usually found in AD with a similar degree of dementia (Hansen *et al*, 1990). Psychiatric symptoms are likely to bias referral towards psychiatric services, while physical problems such as extrapyramidal features may lead to older people being referred more frequently to the geriatric services. This would seem to be our experience.

Therapeutic issues

Until the clinical features of the differing entities are more adequately resolved, some subjects with dementia, especially those who are elderly, will continue to be diagnosed incorrectly as having AD or one of the other dementias when in fact they have cortical LB, and vice versa. This has important implications, as has already become apparent, for the evaluation of new treatments for AD, and emphasises the need for post-mortem verification of the diagnosis in as many trial patients as possible. Accurate clinical classification is important if treatment regimes, anticholinesterase-based or otherwise, are to be evaluated specifically in people thought to have a LBD.

As has been pointed out by others (McKeith *et al*, 1992*b*), there is little doubt that some patients with SDLT are particularly sensitive to neuroleptics, even to the extent of developing the neuroleptic malignant syndrome. Certainly many of them appear to experience significant side-effect profiles at quite low doses.

Can the features of a LBD be treated? That such patients have a significant cholinergic deficit is now well established (e.g. E. K. Perry *et al*, 1990). Some patients subsequently proven to have Lewy body pathology as well as that of AD have been among those responding to an anticholinesterase such as tacrine in clinical trials. This is therefore an avenue worthy of further exploration.

Anti-Parkinsonian treatment does appear to be of modest benefit, especially if combined with physiotherapy, producing a subsequent improvement in mobility, although this is often relatively short-lived. L-dopa and anticholinergic medications do, however, often appear to worsen the cognitive and behavioural features, necessitating the use of low doses of those drugs least likely to aggravate confusion. Benefit has also been reported in a pilot study (Williams *et al*, 1993) in which the difficulties of evaluating treatment approaches for DLBD were helpfully explored.

It has also been reported that clozapine, a novel neuroleptic drug, was effective in treating psychotic symptoms in one patient with DLBD. This remains to be confirmed. Future studies should address the potential risk:benefit ratio when prescribing neuroleptics for this type of disorder.

In conclusion

This is a challenging area of medicine and further work needs to be undertaken before we will properly understand its place in the spectrum of dementia

disorders. Nevertheless, we are even now able to diagnose it clinically, albeit still with inadequate sensitivity and specificity, and are able to start exploring the relevant therapeutic issues.

The old age psychiatrist

> "The greatest difficulty is when weakness and stiffness of limbs come on without the usual attitude and facial expression, and especially if there is also chronic mental failure. I have known the nature of such a case to be either mistaken or mysterious during many years.' (Gowers, 1893)

This statement, applied by Gowers to paralysis agitans (PD), might aptly be applied, in terms of the "mistaken or mysterious" nature, to LBD: mistaken because of diagnostic uncertainty, and mysterious because of nosological uncertainty. What seems less uncertain is that LBD is far from being rare, although a word of caution needs to be given: published case reports number only about 300, and statements about the prevalence of LBD are based (mainly) on highly selected post-mortem series – wherein lies both the mistake and the mystery.

How common is LBD?

A definitive answer is not yet available. Statements about LBD being the second commonest cause of the dementia syndrome should, in my view, be viewed with caution. They are based on studies such as those summarised in Table 1. The frequency of LBD in these series ranges between 4.6% and 21.5%. The lowest frequency is found in studies which consider all autopsies (Forno & Langston, 1988; Lennox *et al*, 1989). I have previously reviewed evidence (Byrne *et al*, 1991*a*) which indicates that the frequency of the different aetiological causes of the dementia syndrome is influenced not only by histological criteria but also by the referring speciality. Jellinger *et al* (1990) showed that AD was found more frequently in the sample from psychiatric hospitals, whereas PD was more frequently found in samples from general medical and geriatric hospital patients. The prevalence *in vivo* is also not known. One study of consecutive psychogeriatric day-hospital patients found 14 of 60 patients with dementia (23.3%) fulfilled clinical operational diagnostic criteria (McKeith *et al*, 1992*a*) for LBD (Ballard *et al*, 1993).

Table 1
Prevalence of LBD in post-mortem series

Reference	*n*	Sample	No. (%) with LBD
Forno & Langston (1988)	260	Consecutive autopsies	12 (4.6)
Lennox *et al* (1989)	216	Consecutive autopsies	15 (6.9)
Joachim *et al* (1988)	150	Ante-mortem diagnosis of dementia	26 (17.3)
Dickson *et al* (1989)	216	Ante-mortem diagnosis of degenerative brain disease	27 (12.5)
R. H. Perry *et al* (1990)	93	Psychiatric hospital patients with dementia	20 (21.5)
Burns *et al* (1990*b*)	50	Patients fulfilling diagnostic criteria for Alzheimer's disease	6 (12)
Galasko *et al* (1994)	170	Ante-mortem diagnosis of possible or probable Alzheimer's disease	42 (24.7)

Clinical features

Although the following description of the clinical features of LBD is drawn from samples from widely different settings, a remarkably consistent 'core' symptom profile emerges. LBD is characterised by dementia, Parkinsonism and neuropsychiatric symptoms; these are detailed in Table 2, together with approximate frequencies. Age may modify these features. Kosaka (1990) described LBD in Japan, and found a younger age of onset was associated with a higher frequency of marked Parkinsonian features.

Table 2
Clinical features of LBD

	Approximate % of patients experiencing symptoms
Dementia	100
'mild' at onset	
marked early visuo-spatial problems	
prominent attention disorder	
Fluctuation in cognition with episodes resembling delirium	80
Parkinsonism	90
Parkinsonism as presenting feature	20–25
rigidity	80
tremor	50
bradykinesia	40
gait disorder	50
postural abnormality (mainly flexed)	30
often described as mild	
Neuropsychiatric	30–50
visual hallucinations, often complex	25
depression	15
paranoid delusions	10

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Age also modifies features in PD: in late-onset PD (after 70 years), rigidity and bradykinesia are more symmetrical, tremor is less marked and L-dopa fluctuation is late and mild when compared with 'classic' PD (Godwin-Austen & Lowe, 1987; Broe, 1992).

The fluctuation in cognition in LBD when it occurs early in the course of the condition can be said to be characteristic. The fluctuation can be observed within a day and from day to day (Williams *et al*, 1993), this may reflect the prominent attentional disorder of the condition. Superimposed on this fluctuating level of cognitive function are acute confusional states (ACS), which are idiopathic, unrelated to the common causes of ACS in the elderly. A patient with dementia who is having frequent ACS (not limited to nocturnal occurrence) for which no cause is found should be suspected of having LBD.

Similarly, although psychiatric features are common in AD (Burns *et al*, 1990*a*), early prominent hallucinations (especially visual) or delusions should suggest LBD. Less common symptoms of LBD include autonomic dysfunction, myoclonus, supranuclear palsy, polydipsia, dyskinesia, chorea, lower motor neurone signs (fasciculation, muscle wasting), dysarthria (common in patients with marked Parkinsonian features) and dysphagia.

There are now validated operational clinical diagnostic criteria for the diagnosis of LBD. The Newcastle criteria (McKeith *et al*, 1992*a*) require fluctuation in cognitive level which persists over a long period (weeks or months) and is associated with one of: visual or auditory hallucinations, mild spontaneous extrapyramidal features or neuroleptic sensitivity syndrome, repeated falls, and transient clouding or loss of consciousness. The Nottingham criteria (Byrne *et al*, 1991*b*) give clinical criteria for two levels of probability: *probable* where dementia with or without marked fluctuation in cognition is associated with unequivocal Parkinsonian symptoms at some point in the cause of illness; *possible* where dementia is associated with equivocal or mild Parkinsonian features. Both these criteria have satisfactory reliability and specificity but are only moderately sensitive (Byrne, 1994; McKeith *et al*, 1994*a*). McKeith *et al* (1994*b*) in their validation study provide a useful discussion of the potential reasons for misdiagnosis of LBD. Table 3 summarises some of the key features in the differential diagnosis of LBD from AD, vascular dementia (VD), and CJD.

Some believe that LBD is a subtype of AD (Hansen *et al*, 1990; Förstl *et al*, 1993), and in some cases it can be difficult to distinguish the two conditions.

Table 3
Differential diagnosis of LBD (revised from Byrne, 1992)

Features	LBD	VD	AD	CJD
Cognition at onset	Mildy impaired, prominent attentional problems may be normal	Patchy impairment	Impaired, prominent memory problems	Impaired, may be focal
Fluctuation in cognition	Early and sustained	Marked at night relative day-time lucidity	Rare	Not marked
Plateau of stable cognition	Very rare	Common	Rare	Very rare
Parkinsonism	Almost invariably mild in old, may be presenting feature and resemble PD	Rarely resembles PD. Gait disorder prominent	Rarely resembles PD, rigidity prominent	May occur
Psychiatric symptoms	Common	Depression common	Common but rarely early featues	Not marked
Myoclonus	Relatively rare and 'mild'	Very rare	May occur	Common
Epilepsy	Not described	Common	Quite common	Quite common
Course	Variable	Stepwise or gradual	Gradual	Rapid
Duration (average)	3–8 years	2–5 years	4–9 years	½–2 years
Sex ratio	? Male>female	Male>female	Female>male	No difference

LBD, Lewy body dementia; VD, vascular disease; AD, Alzheimer's disease; CJD, Creutzfeldt–Jakob disease; PD, Parkinson's disease.

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Crystal *et al* (1990) suggest that EEG may be helpful – in LBD, EEG change occurs early in the course, whereas EEG may be normal in the early stages of AD.

Even in 'Alzheimered' LBD (cases in which Alzheimer histological change coexists with cortical and brainstem LB) neuroleptic sensitivity (McKeith *et al*, 1992*b*) exists.

Until the NINDS–AIRENS (Roman *et al*, 1993) criteria for the diagnosis of VD were proposed, the Hachinski Ischaemia Scale (IS; Hachinski *et al*, 1975) was widely used as an aid to diagnosis. As McKeith *et al* (1994*a*) have pointed out, the fluctuation and mild cognitive change (features of LBD) may lead to high scores on the IS in patients with LBD. The fluctuation in VD is typically nocturnal worsening with relative daytime lucidity (Wade & Hachinski, 1987) and the plateaux of stable cognition in VD are rare in LBD. Some cases of LBD have myoclonus and triphasic waves on the EEG associated with a rapidly progressive clinical course (Burkhardt *et al*, 1988; Byrne *et al*, 1989). The myoclonus in LBD is not as severe as in CJD, nor is there an exaggerated startle reflex. Ataxia is not a feature of LBD, whereas it is common in CJD.

There are many other causes of dementia with Parkinsonism (see Lennox, 1992), most of which, such as Huntington's chorea or multiple system atrophy, have characteristic neurological symptoms. The clinical syndrome associated with progressive supranuclear palsy may occasionally be due to LBD (Fearnley *et al*, 1991).

Management

In cases where Parkinsonian features are severe and disabling, anti-Parkinsonian agents may be given a therapeutic trial. There is always a trade-off between the benefit of improved mobility, the release of behaviours that may ensue (such as wandering), and the mental state, especially if psychotic symptoms are present.

One small pilot study of an open trial of the use of anti-Parkinsonian medication detailed the potential problems but reported some benefit (Williams *et al*, 1993).

Old people do not require as much L-dopa as their more youthful counterparts (Broe & Caird, 1973). It is worth getting an estimate of the shifting baseline for each individual patient – as motor, cognitive and psychotic symptoms are variable over time – before commencing any treatment. An empirical approach is recommended: start low and titrate the dose according to both motor and mental-state changes. Recommended starting doses include:

(a) Anti-Parkinsonian agents – L-dopa (100 mg) and carbidopa (10 mg) as Sinemet 110 (half a tablet twice a day), co-beneldopa (50 mg) and benserazide (12.5 mg) as Madopar 62.5 (one tablet twice a day), and L-deprenyl (5 mg daily); Broe & Caird (1973) described such a low titrated dose of L-dopa in elderly demented patients with Parkinsonism and report benefit.

(b) drugs to treat psychotic symptoms – chlormethiazole (192–384 mg daily), and lorazepam (1–2 mg twice a day, short-term use only)

(c) Neuroleptics with extreme caution – thioridazine (10 mg twice a day), sulpiride (100–200 mg daily); neuroleptic sensitivity is a problem, but we have encountered it much less frequently than the Newcastle group (Byrne *et al*, 1992), possibly because our routine dosage of neuroleptics is much lower.

The novel antipsychotics (such as clozapine) have been used with benefit in LBD (Abelskov & Torpdahl, 1993) but clozapine has to be carefully monitored for adverse effects and is expensive. Some suggest that chlormethiazole has a neuroprotective effect (Cross *et al*, 1991; Baldwin *et al*, 1993). In LBD its use is empirical but was suggested by its efficacy in delirium tremens. Some patients experience breakthrough of psychotic symptoms on long-term treatment.

Discussion

The primary aim of this article is to compare and contrast the views of specialists in neurology, psychiatry of old age, and geriatric medicine. In general, the contributors are in broad agreement about the clinical profile of patients with cortical LBD, although there are some differences between them which are perplexing. Thus, for example, hallucination rates appear to be higher in neurological practice (up to 50%) whereas Parkinsonism is seen in the majority (90%) of cases coming to old age psychiatry – although seldom as a presenting feature, usually falling short of the classic triad of bradykinesia, rigidity and tremor, and probably often exacerbated by neuroleptics. These are certainly not the skews in symptom rates which one would predict on the basis of speciality referral bias. A likely partial explanation is that all three contributors are experts in the field of dementia, and their reviews may reflect this aspect of their practice rather more than mirroring the general experience and knowledge

within their main speciality. Standardised methods for eliciting and recording individual symptoms in this group of patients have not yet been developed, and in their absence further interpretation of the different reported symptom rates would be highly speculative.

Nevertheless, it is of particular interest to our group in Newcastle that syncope and falls have not been generally identified in these reviews as primary characteristics of LBD. Up to one-third of our autopsy-confirmed cases of SDLT had repeated unexplained falls at the time of clinical presentation, and these were often a significant problem in the patients' management. We have previously speculated that spontaneous fluctuations in level of consciousness and abnormalities in posture, balance and gait secondary to nigrostriatal dysfunction or central baroreceptor reflex dysfunction, may be contributory patho-physiological mechanisms. Whether or not syncope and falls are important manifestations of LBD needs to be further clarified – Ballard *et al* (1993) found that 15 out of 16 (94%) demented patients with idiopathic clouding of consciousness had experienced frequent falls, and 14 of these met Newcastle criteria for SDLT.

Both Dr Galasko and Professor Wilcock have made detailed reference to the overlap between Alzheimer-type and LB pathology in these patients. Until recently PD and AD were considered to be clinically separate disorders and the possibility that their pathologies may be inter-related poses some fundamentally challenging questions for clinical classification. Some light may be shed on this pathological relationship by the results of apolipoprotein E genotyping which suggest that possession of one or more $\epsilon 4$ alleles is a risk factor, not only for late-onset familial sporadic AD, but also for LBD, with an $\epsilon 4$ allele frequency of 35–40% in both disorders compared with 14–17% in controls (Benjamin *et al*, 1994). Apolipoprotein E4 may exert its pathoplastic effect by decreasing the solubility of β-amyloid and predisposing to the formation of diffuse SP. The observation that PD patients without dementia and without Alzheimer-type pathology have normal $\epsilon 4$ allele frequencies raises the possibility that β-amyloidosis may be a secondary feature of LBD and its expression at least partially influenced by differential apolipoprotein metabolism.

Returning to clinical issues, Dr Byrne has emphasised the methods currently available for clinical diagnosis, including the role of investigations. Although cognitive fluctuation is undoubtedly a characteristic of many of these patients, it is difficult to define, particularly in the later stages of illness, when persistent and profound cognitive impairment may supervene. By contrast, the intermittent acute confusional states to which Dr Byrne makes reference are usually more easily recognised. Ballard *et al* (1993) found a question from the CAMDEX rating scale – "are there episodes lasting days or weeks when his/her thinking seems quite clear and then becomes muddled?" – useful in identifying fluctuation. There is as yet little systematic information available about the role of investigative procedures in differential diagnosis – our experience with EEG is that slowing of the dominant rhythm occurs earlier and more often in LBD than in AD.

Despite the nosological and diagnostic uncertainties, there do seem to be some general principles emerging about the management of these patients. The recognition of their unusual and fluctuating symptom profile needs to be explained to carers, and the possibility of rapid decline and a worse prognosis borne in mind. Motor symptoms may well be relieved by standard anti-Parkinsonian treatments in appropriate low dose. Patients who are not distressed by their hallucinations may accept them as the cost of improved mobility – a therapeutically more satisfying outcome than having to render a patient immobile in order to diminish frightening or distressing psychotic symptoms. Neuroleptic drugs are not absolutely contraindicated in LBD, but recent Committee on the Safety of Medicines guidelines suggest that they should be used with extreme caution because of their propensity to induce acute and life-threatening deterioration in some cases. Several alternative strategies have been suggested – recent case reports (Lee *et al*, 1994; Allen *et al*, 1995) describe gratifying remissions of psychotic symptoms in response to risperidone, which has high affinity 5-HT_2 and D_2 antagonist properties. Extrapyramidal side-effects and severe neuroleptic sensitivity may however also occur with risperidone and systematic trials are required to establish whether safe and efficacious dosing regimes are possible.

In conclusion, one must say that clinicians, be they old age psychiatrists, geriatricians or neurologists, should not feel that they are being asked to deal with a new disorder. Review of our old autopsy material suggests that such patients were equally common three decades ago, but went unrecognised. What has happened is that improved neuropathological methods (e.g. antiubiquitin immunocytochemical staining of cortical LB) have revealed the disorder and led us to a point where we have the potential clinically to diagnose and treat demented patients more precisely. In order to proceed we must improve our methods of defining and measuring relevant psychopathology

and neurological abnormality in demented patients. The terminology and tools of general psychiatry and neurology may need extensive modification if we are to succeed. Research and clinical collaboration across and between the specialities will undoubtedly help to further this process.

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