Diagnosing dementia with Lewy bodies: new diagnostic criteria

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Title Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium

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Summary

Diagnostic criteria for dementia with Lewy bodies (DLB) have been presented in three previous publications from the DLB Consortium,[1–3] the last appearing 12 years ago. Since then, understanding of DLB has steadily developed, prompting this further revision. As with consensus diagnostic criteria for other neurodegenerative disorders, such as Alzheimer's disease (AD),[4,5] the incorporation of diagnostic biomarkers alongside clinical features has been emphasised.

Dementia remains an essential clinical prerequisite for diagnosis. Cognitive domains particularly affected in DLB are attention, visuoperceptual abilities, and executive function. There is relative preservation of mnemonic function in the early stages of DLB, unlike the situation in most cases of AD, but no DLB-specific cognitive screening instrument has yet been described.

As previously, clinical features other than dementia are weighted as 'core' or 'supportive' for the diagnosis of DLB. Biomarkers are weighted as 'indicative' or 'supportive'. DLB diagnosis is categorised as either 'probable' or 'possible', dependent upon the number of core clinical features and indicative biomarkers which are present.

The core clinical features category retains the three key features of previous criteria, namely fluctuating cognition (variations in attention or alertness) and visual hallucinations, both typically occurring early in the disease course, and one or more of the spontaneous cardinal features of parkinsonism (bradykinesia, rest tremor, rigidity) although it is acknowledged that these may not occur or be prominent in the early stages. To the core clinical features category is now added rapid eye movement sleep behaviour disorder (REMBD), sometimes known as 'dream enactment', more usually reported by the bed partner than by the patient, which may precede the other features of DLB by many years. (REMBD may also occur in other synucleinopathies, such as Parkinson's disease [PD] and multiple system atrophy.)

Supportive clinical features, commonly present and sometimes seen early in the course, as previously include neuroleptic sensitivity, postural instability and falls, autonomic dysfunction, and psychotic features (hallucinations in sensory modalities other than visual, systematised delusions). New features in this group include hypersomnia (excessive daytime somnolence) and hyposmia.

Indicative biomarkers are: reduced dopamine transporter uptake in the basal ganglia as demonstrated by SPECT or PET imaging; reduced uptake on ^{123}iodine-MIBG myocardial scintigraphy indicating impaired postganglionic sympathetic cardiac innervation; and polysomnography to confirm REM sleep without atonia, a cardinal feature of REMBD.

Supportive biomarkers are: relative preservation of medial temporal lobe structures on structural brain imaging (i.e. CT or MRI), unlike the typical findings in AD; generalised low uptake on functional brain imaging (i.e. SPECT perfusion or PET metabolism scan), with reduced occipital activity, and relative preservation of posterior or mid-cingulate metabolism on FDG-PET (the 'posterior cingulate island sign'); and prominent posterior slow-wave EEG activity with periodic fluctuations in the pre-alpha/theta range. To date,

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no blood, cerebrospinal fluid, peripheral tissue or genotype biomarkers for DLB are available.

Probable DLB may be diagnosed if there are two or more core clinical features present, or just one core clinical feature but with one or more indicative biomarkers. Probable DLB cannot be diagnosed on the basis of biomarkers alone. Possible DLB may be diagnosed if there is one core clinical feature but with no indicative biomarkers, or if there is one or more indicative biomarker but no core clinical features.

Supportive clinical features and biomarkers do not feature in the diagnostic criteria for either probable or possible DLB.

DLB should be differentiated from the dementia which occurs in established PD, although both may be encompassed by the rubric of 'Lewy body dementias' and probably share a similar pathophysiology.[6] At time of writing, PD dementia is a licensed (i.e. NICE-approved) indication for treatment with cholinesterase inhibitors in the UK, whereas DLB is not licensed, although pragmatically many clinicians will use these drugs off-licence in cases of DLB.

Opinion

Generally these new diagnostic criteria for DLB are to be welcomed. They form the latest chapter in attempts to raise the clinical profile of DLB. Twenty-five years ago, DLB was included in a volume entitled 'Unusual dementias', although the author pointed out that DLB was probably not uncommon, although often overlooked.[7] Many studies in the interim have raised the clinical profile of DLB, and the work of the DLB Consortium has resulted in three previous publications on proposed diagnostic criteria.[1–3] It should be emphasised that this is not some sterile academic exercise in differential diagnosis for ivory tower neurologists, since DLB may be encountered in its various guises by general practitioners, general physicians, geriatricians, and psychiatrists. Moreover, misdiagnosis of DLB may have potentially serious, even life threatening, consequences for patients (e.g. inappropriate prescription of neuroleptics). The less favourable prognosis of DLB compared to AD[8] may inform the development of appropriate care packages.

Studies will now be required to measure the sensitivity and specificity of these criteria, ultimately with the diagnosis confirmed pathologically (this paper also includes recommendations for minor modifications to pathological methods and criteria for DLB), to assess their utility. For example, the 'Possible DLB' category seems rather broad, since anyone with dementia and either REMBD or parkinsonism would qualify. Such a formulation may ensure high diagnostic sensitivity, but possibly at a price of many false positives, a calculus which many clinicians may tolerate or even favour as it should ensure low numbers of false negatives (i.e. missed diagnoses). However, if the hope is that these criteria may facilitate further trials of therapeutic (hopefully disease-modifying) agents in DLB, criteria with high specificity may be preferred by researchers to ensure that no false positives are randomised, which may carry a risk of diluting any possible treatment effect (as may have happened in some AD therapeutic trials in which false positives, i.e. individuals without AD, were inadvertently included).

It may be noted that these proposed criteria are most suitable for use in tertiary care and research settings. Investigations such as dopamine transporter scans, MIBG scintigraphy, and polysomnography, necessary for the identification of indicative biomarkers, may not be readily available in many centres. Criteria suitable for low resource settings, presumably dependent only on core clinical features, may also be required.

Dementia remains a sine qua non for DLB diagnosis, as reflected in the name of the condition. However, the evidence that REMBD may precede DLB by many years, even decades,[9] indicates there may be a long prodromal phase to the disorder, at least in some patients. It remains unclear how the pre-dementia phase of this condition should be designated. Since 'mild cognitive impairment' (MCI) has been used in the past by some clinicians as equivalent to prodromal AD, perhaps 'MCI-DLB' might be used (as in the clinic of one of the authors [AJL]), analogous to the construct of PD-MCI preceding PDD,[10] although this would retain the 'dementia' tag which is not appropriate in these circumstances. Another option might be Lewy body-MCI, to reflect the underlying pathology. Whatever the name, this is surely the group in which the deployment of disease-modifying drugs, if such become available, would be most pressing, in the hope that early intervention might result in dementia prevention.

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