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COMMENTARY

Lewy body dementias: One spectrum or two diseases?

Varsha Ratan Gaikwad[1] | Sakshi Tyagi[2] | Ambika Nand Jha[2]

[1] Department of Pharmaceutical Sciences, Sandip University, Nashik, Maharashtra, India
[2] Department of Pharmacy, Sharda University, Greater Noida, Uttar Pradesh, India

Correspondence
Ambika Nand Jha
nandjha99@gmail.com

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Responsible editor
M Mostafa Zaman
0000-0002-1736-1342

Reviewers
Subash Kanti Dey
0000-0002-0581-0681
Gopen Kumar Kundu
0000-0002-1226-4885

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Lewy body dementias, encompassing dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), are the second most common form of neurodegenerative dementia following Alzheimer's disease. Although both syndromes are unified by the pathological hallmark of α–synuclein deposition, their clinical classification remains bifurcated, defined not by distinct mechanisms but by the order in which cognitive and motor symptoms emerge [1]. This longstanding convention, based on an arbitrary temporal rule, is increasingly challenged by overlapping presentations and shared pathophysiological features. The central question remains: Are DLB and PDD distinct entities or phenotypic variants within a broader, continuous disease spectrum? The current diagnostic framework distinguishes DLB and PDD based on a one-year rule: if cognitive impairment precedes or appears within a year of Parkinsonism, DLB is diagnosed; if dementia occurs later in the course of Parkinson's disease, PDD is assumed. However, this artificial cutoff has little biological basis and often fails in real-world clinical contexts, where symptom onset may be subtle, fluctuating, or ambiguously reported [2]. As a result, many patients fall into diagnostic grey zones, impacting both prognosis and treatment decisions. Clinically, both forms of LBD share core features: fluctuating cognition, REM sleep behaviour disorder, visual hallucinations, and parkinsonism-supported by converging evidence from neuroimaging, biomarker studies, and therapeutic response.

Structural and functional imaging studies have identified overlapping patterns of cortical and subcortical involvement, particularly in dopaminergic and cholinergic networks. Post-mortem studies consistently demonstrate widespread α–synuclein pathology in both DLB and PDD, often accompanied by Alzheimer-type changes such as β–amyloid plaques and tau tangles [3]. These shared pathologies correlate with cognitive decline, psychiatric symptoms, and disease progression in both conditions.

Despite these parallels, the temporal distinction remains entrenched in diagnostic criteria issued by the DLB Consortium and the Movement Disorder Society [4]. While useful for clinical categorisation, this model fails to capture the heterogeneity observed across patients and may hinder research by segregating patients with biologically similar diseases. For instance, patients with early psychiatric symptoms and later motor dysfunction may be mislabeled, resulting in suboptimal treatment strategies and exclusion from relevant clinical trials [4]. Importantly, the therapeutic landscape for LBDs also reflects a spectrum-based reality. Both DLB and PDD respond to cholinesterase inhibitors for cognitive and neuropsychiatric symptoms, while dopaminergic agents address motor features [5]. To better understand the distinction between the two diagnostic approaches and their clinical implications, refer to **Table 1**, which contrasts the conventional model with the emerging continuum model, emphasising how a unified approach can guide more personalised therapies. However, the risk of exacerbating psychosis with dopaminergic therapy in

Key messages

Recognising Lewy body dementias as a singular, heterogeneous spectrum rather than as two distinct diagnoses aligns with current neuropathological and biomarker evidence. Abandoning rigid temporal classifications could enhance diagnostic precision, optimise therapeutic decisions, and facilitate inclusion in targeted clinical trials, paving the way for biologically driven, individualised approaches in neurodegenerative disease management.

Table 1 Conventional versus emerging models in Lewy body dementias

Aspect	Conventional dichotomous model	Emerging continuum model
Disease Classification	Dementia with lewy bodies (DLB): Cognitive decline manifests prior to or within 12 months of motor symptom onset. Parkinson's disease dementia (PDD): Dementia emerges after at least one year of established Parkinsonism.	Disease is conceptualised as a spectrum with overlapping onset of cognitive, motor, psychiatric, and sleep disturbances. No distinct temporal order governs the presentation of symptoms.
Neuropathology	Predominantly characterised by α-synuclein deposits. DLB often demonstrates more prominent cortical involvement, while PDD predominantly affects subcortical structures.	Extensive cortical and subcortical involvement of α-synuclein pathology in both DLB and PDD. Coexistent Alzheimer-type pathologies (β-amyloid plaques, tau tangles) observed across both entities, suggesting shared neurodegenerative processes.
Clinical Features	Cognitive impairment follows motor symptom onset in PDD, whereas DLB exhibits early cognitive symptoms. Both conditions feature Parkinsonism, visual hallucinations, fluctuating cognition, and REM sleep behaviour disorder (RBD).	A broader clinical continuum of cognitive, motor, psychiatric, and sleep disturbances with no rigid sequence, indicating that cognitive and motor symptoms may emerge simultaneously or in varying order. Common pathophysiological markers overlap between both forms of LBD.
Diagnostic Thresholds	Clear temporal distinction based on the onset of dementia relative to motor features, specifically the one-year cutoff rule for PDD.	Diagnostic boundaries are fluid, guided by clinical, pathological, and molecular markers rather than an arbitrary time frame. Both phenotypes represent variations within a spectrum.
Therapeutic Implications	Cholinesterase inhibitors and dopaminergic therapies are commonly employed, but treatment regimens are often stratified based on the temporal progression of symptoms, without regard for underlying pathophysiology.	A unified therapeutic approach tailored to individual patient profiles using biomarkers. Both cholinesterase inhibitors and dopaminergic agents are employed but with careful consideration of the individual patient's symptomatology and the risk of treatment-related side effects.
Clinical Trial Design	Clinical trials often restrict inclusion based on rigid diagnostic criteria, such as the one-year temporal cutoff, potentially excluding individuals with early cognitive or psychiatric symptoms and misclassifying patients.	Clinical trials are designed to accommodate the full spectrum of disease, focusing on biomarker-based phenotyping rather than rigid temporal criteria, allowing for more inclusive patient selection and better representation of disease variability.

both groups underscores the need for a nuanced approach. As research moves toward disease-modifying treatments, particularly those targeting α–synuclein aggregation, rigid classifications based solely on symptom chronology could limit therapeutic reach and precision. Increasingly, experts advocate for a unified model of Lewy body disorders that integrates clinical, pathological, and molecular data. Biomarker studies-spanning cerebrospinal fluid analysis, PET imaging, and genetic profiling-are beginning to delineate shared and subtype-specific signatures [6]. A shift toward biologically informed classification could enhance diagnostic accuracy, guide personalised therapy, and improve clinical trial design by accommodating the true complexity of disease presentation. Revisiting the current nosology is not simply a matter of semantics but a call for a paradigm shift in neurodegenerative disease research and care [7]. Recognising LBDs as a spectrum-rather than two arbitrarily separated diseases-aligns classification with emerging biological understanding and paves the way for more tailored, effective interventions.

A spectrum-based model of Lewy body dementia can improve diagnostic clarity, personalise therapeutic strategies, and reflect the complex neurobiology of the disease.

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Manuscript drafting and revising it critically: ANJ, VRG, ST. *Approval of the final version of the manuscript:* VRG, ST, ANJ. *Guarantor of accuracy and integrity of the work:* VRG, ANJ.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

Not applicable

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