BRAIN. Broad Research in Artificial Intelligence and Neuroscience
e-ISSN: 2067-3957 | p-ISSN: 2068-0473
Covered in: Web of Science (ESCI); EBSCO; JERIH PLUS (hkdir.no); IndexCopernicus; Google Scholar; SHERPA/RoMEO; ArticleReach Direct; WorldCat; CrossRef; Peeref; Bridge of Knowledge (mostwiedzy.pl); abcdindex.com; Editage; Ingenta Connect Publication; OALib; scite.ai; Scholar9; Scientific and Technical Information Portal; FID Move; ADVANCED SCIENCES INDEX (European Science Evaluation Centre, neredataltics.org); ivySCI; exaly.com; Journal Selector Tool (letpub.com); Citefactor.org; fatcat!; ZDB catalogue; Catalogue SUDOC (abes.fr); OpenAlex; Wikidata; The ISSN Portal; Socolar; KVK-Volltitel (kit.edu)
2026, Volume 17, Issue 3, pages: 369-380
Submitted: June 27th, 2026 | *Accepted for publication:* August 16th, 2026

Artificial Intelligence in Dementia with Lewy Bodies — Current Applications, Diagnostic Challenges, and Future Perspectives

Maria Ciubotaru
Faculty of Biology, "Alexandru Ioan Cuza" University of Iasi, Romania.
ciubotarumaria1234@gmail.com,
https://orcid.org/0009-0000-1428-2457

Laura Romilă
"Ioan Haulica" Institute, Apollonia University, Iasi, Romania.
laura.dartu@gmail.com

Alin Ciobica
Faculty of Biology, "Alexandru Ioan Cuza" University of Iasi, Romania. "Ioan Haulica" Institute, Apollonia University, Iasi, Romania;
"Olga Necrasov" Center, Biomedical Research Group, Romanian Academy, Iasi, Romania; Academy of Romanian Scientists, Bucharest, Romania.
alin.ciobica@uaic.ro,
https://orcid.org/0000-0002-1750-6011

Mihai Hogas*
University of Medicine and Pharmacy, "Grigore T. Popa", Iași, Romania.
mihaimmh@yahoo.com,
https://orcid.org/0000-0002-8501-7279

Bogdan Novac*
University of Medicine and Pharmacy, "Grigore T. Popa", Iași, Romania.
bogdannvc@gmail.com,
https://orcid.org/0000-0003-4501-1718

Ancuta Miler
University of Medicine and Pharmacy, "Grigore T. Popa", Iași, Romania.
miler.ancuta@umfiasi.ro,
https://orcid.org/0009-0001-0709-6899

Ecaterina Tomaziu-Todosia Anton
University of Medicine and Pharmacy, "Grigore T. Popa", Iași, Romania.
tomaziu-todosia.ecaterina@d.umfiasi.ro, https://orcid.org/0009-0004-8547-4156

Otilia Novac
University of Medicine and Pharmacy, "Grigore T. Popa", Iași, Romania.
otilia76@gmail.com, https://orcid.org/0000-0002-4708-3603

Adrian Cantemir
University of Medicine and Pharmacy, "Grigore T. Popa", Iași, Romania.
adrian.cantemir@gmail.com

**Corresponding authors*

Abstract: *Dementia with Lewy bodies (DLB) is a clinically and biologically heterogeneous neurodegenerative disorder characterised by cognitive impairment together with variable combinations of cognitive fluctuations, recurrent visual hallucinations, rapid eye movement sleep behaviour disorder, parkinsonism, autonomic dysfunction, and other neurological and neuropsychiatric manifestations. Diagnostic uncertainty remains substantial because DLB overlaps clinically with Alzheimer's disease (AD), Parkinson's disease dementia, vascular cognitive impairment, and other neurodegenerative disorders, while mixed neuropathology is common. Artificial intelligence (AI), including machine-learning and deep-learning approaches, offers an opportunity to integrate heterogeneous clinical, neuropsychological, neuroimaging, molecular, electrophysiological, and longitudinal data. Current research has investigated AI for differential diagnosis, neuroimaging analysis, multimodal biomarker integration, prodromal risk prediction, prognosis, and digital monitoring. More recently, multimodal biomarker studies in mild cognitive impairment with Lewy bodies have suggested that combinations of MRI, EEG, and plasma markers may provide additional prognostic information beyond cognitive testing alone. However, these findings should not be interpreted as evidence that AI is ready for autonomous clinical diagnosis. Explainable AI may improve transparency and facilitate clinical interpretation, but explanations themselves require validation and should not be regarded as evidence of causality. Future research should prioritise large multicentre longitudinal cohorts, biologically informed reference standards, multimodal and federated learning, calibrated probabilistic prediction, digital biomarkers, and prospective evaluation of clinical utility.*

Keywords: *dementia with Lewy bodies; artificial intelligence; machine learning; deep learning; neuroimaging; biomarkers; α-synuclein.*

How to cite: Ciubotaru, M., Romilă, L., Ciobica, A., Hogas, M., Novac, B., Miler, A., Tomaziu-Todosia Anton, E., Novac, O., & Cantemir, A. (2026). Artificial intelligence in dementia with Lewy bodies—Current applications, diagnostic challenges, and future perspectives. *BRAIN. Broad Research in Artificial Intelligence and Neuroscience*, *17*(3), 369-380. https://doi.org/10.70594/brain/17.3/22

1. Introduction

Dementia with Lewy bodies (DLB) is one of the major neurodegenerative causes of dementia and is characterised by a combination of cognitive impairment, fluctuations in attention and alertness, recurrent visual hallucinations, rapid eye movement sleep behaviour disorder (RBD), spontaneous parkinsonism, autonomic dysfunction, and other supportive clinical manifestations. The clinical phenotype is heterogeneous, and the relative contribution of cognitive, motor, sleep, autonomic, and neuropsychiatric manifestations varies considerably between individuals (McKeith et al., 2017; Neupane & Hortobágyi, 2025).

This heterogeneity creates substantial diagnostic challenges. DLB may overlap clinically with Alzheimer's disease (AD), Parkinson's disease dementia (PDD), vascular cognitive impairment, frontotemporal degeneration, and other causes of cognitive decline. In addition, patients may present with mixed neuropathology, particularly combinations of Lewy body and AD-related pathology. Consequently, the clinical diagnosis does not necessarily correspond to a single underlying pathological process (McKeith et al., 2017; Barba et al., 2024).

The development of biomarkers has progressively changed the diagnostic landscape. Neuroimaging, dopamine-transporter imaging, cardiac sympathetic imaging, electrophysiological measures, and, more recently, α-synuclein seed amplification assays have provided additional evidence supporting the identification of Lewy body disease. The emergence of α-synuclein seed amplification assays is particularly important because these methods aim to detect pathological α-synuclein directly rather than relying exclusively on clinical manifestations or indirect biomarkers (Kuang et al., 2024; Bregendahl et al., 2025; Kaya et al., 2026). Recent meta-analytic evidence indicates encouraging diagnostic performance of α-synuclein seed amplification assays, although substantial methodological variation remains between laboratories and sample types (Hasoon et al., 2026).

At the same time, the increasing availability of multimodal clinical and biological information creates a computational challenge. Conventional clinical assessment requires clinicians to integrate numerous variables that may differ in reliability, timing, and biological meaning. Artificial intelligence (AI) may assist by identifying complex relationships between variables and by combining information from multiple domains (Borchert et al., 2023; Hefnawy et al., 2025).

AI encompasses a broad range of computational methods, including classical machine learning (ML), deep learning, neural networks, ensemble methods, and other approaches capable of extracting predictive patterns from complex datasets. In DLB, these techniques have been investigated primarily for diagnosis and neuroimaging analysis, but their potential applications increasingly extend towards prodromal detection, prognostic prediction, biomarker integration, explainable decision support, and longitudinal monitoring (Borchert et al., 2023; Diab et al., 2025; Hefnawy et al., 2025).

The objective of this review is not to present AI as an established diagnostic solution, but to examine its potential role across the DLB disease continuum while emphasising the methodological and clinical limitations that must be addressed before widespread implementation.

This article presents a narrative review of current and emerging applications of AI in DLB. The literature was selected to provide a clinically oriented overview of studies addressing AI-assisted differential diagnosis, neuroimaging analysis, integration of clinical and biomarker data, early detection, prognosis, and potential applications in precision neurology. Particular emphasis was placed on DLB-specific studies and recent publications illustrating the methodological and clinical challenges of applying AI in this population. Relevant literature was identified through targeted searches of major biomedical databases and reference tracking. The literature search was conducted between July 2025 and August 2026 using PubMed/MEDLINE, Scopus, and Web of Science, complemented by Google Scholar searches. Studies were selected based on their relevance to the scope of this narrative review, with priority given to peer-reviewed publications addressing AI, machine learning, neuroimaging, biomarkers, prognosis, and clinical aspects of DLB.

2. Clinical and Biological Complexity of Dementia with Lewy Bodies

DLB is characterised by a distinctive but heterogeneous clinical syndrome. The fourth consensus report of the DLB Consortium identified fluctuating cognition, recurrent visual hallucinations, REM sleep behaviour disorder, and spontaneous parkinsonism as core clinical features (McKeith et al., 2017).

The recognition that Lewy body disease can become clinically apparent before dementia has also led to the concept of prodromal DLB. Research criteria include mild cognitive impairment with Lewy bodies (MCI-LB), delirium-onset presentations, and psychiatric-onset presentations (McKeith et al., 2020).

The biological substrate of DLB is similarly complex. Pathological α-synuclein accumulation represents a defining feature of Lewy body disease, but amyloid-β and tau pathology may coexist and may influence clinical phenotype and progression. Recent biomarker studies have demonstrated that AD and Lewy body pathology can be identified concurrently in vivo, including in patients whose clinical presentation may initially suggest only one disease process (Baiardi et al., 2024; Barba et al., 2024).

This heterogeneity creates an important opportunity for AI. A conventional diagnostic framework may ask whether an individual fulfils clinical criteria for DLB. A multimodal AI model could provide a more nuanced output, estimating separately the probability of synucleinopathy, AD co-pathology, a DLB clinical phenotype, and future cognitive or functional decline. Such an approach would be particularly relevant to patients with mixed pathology. Rather than forcing an individual into a single diagnostic category, AI could generate a multidimensional biological and prognostic profile (Scott et al., 2022; Borchert et al., 2023; Simuni et al., 2024).

3. Current Applications of AI in DLB

3.1. AI-Assisted Differential Diagnosis

One of the most extensively investigated applications of AI in DLB is automated differential diagnosis. Machine-learning algorithms have been applied to clinical variables, neuropsychological measures, neuroimaging, EEG, and combinations of these data (Borchert et al., 2023; Hefnawy et al., 2025).

A feasibility study by McCombe et al. (2022) demonstrated that machine-learning approaches could distinguish DLB from AD using heterogeneous clinical and biological information. Importantly, the investigators used interpretable association-rule-based classifiers rather than relying exclusively on a black-box deep-learning model. This illustrates the potential value of models that can identify combinations of clinical characteristics contributing to classification.

The clinical relevance of such approaches lies primarily in difficult differential diagnoses rather than in distinguishing advanced DLB from healthy controls. In practice, the most useful AI system would be expected to assist with cases in which the clinical phenotype is incomplete or overlapping (Borchert et al., 2023; McKeith et al., 2017).

Table 1 summarises selected representative studies investigating AI and ML approaches for the diagnosis and differential diagnosis of dementia with Lewy bodies. The studies were selected to illustrate key methodological approaches explored in this field, including interpretable machine learning based on heterogeneous clinical and neuropsychological data, deep learning applied to 18F-FDG PET imaging, and deep-learning approaches addressing diagnostic heterogeneity and mixed pathology. The table is intended to provide an illustrative overview of the current evidence rather than an exhaustive systematic summary of all published studies.

Table 1. AI-based approaches for diagnosis and differential diagnosis of DLB

Study	Population	Data / AI approach	Clinical question	Validation	Main performance / finding
McCombe et al. (2022)	33 participants (17 DLB, 16 AD)	Clinical, neuropsychological and biological/imaging data; interpretable ML	DLB vs AD	LOOCV; no external validation	Accuracy 94%; out-of-sample accuracy 80.5%. Feasible discrimination using heterogeneous features
Etminani et al. (2022)	757 participants	18F-FDG PET; 3D deep learning	DLB vs AD, MCI-AD and controls	90% development / 10% independent test set; no external validation	AUC 96.2%; sensitivity 86%; specificity 100%; F1 92%
Kim et al. (2026)	277 participants; additional ADNI cohort (n = 618)	18F-FDG PET; deep learning ensemble	AD vs DLB vs mixed pathology vs controls	20% independent test set; external validation in ADNI	AUROC 0.90 for DLB; performance decreased in the biomarker-defined ADNI cohort

3.2. Neuroimaging-Based AI

Neuroimaging is particularly suitable for computational analysis because it contains high-dimensional spatial information that may be difficult to evaluate consistently using visual inspection alone. FDG-PET has been one of the most extensively investigated modalities (Kim et al., 2026). Etminani et al. (2022) developed a three-dimensional deep-learning model using FDG-PET to distinguish DLB, AD, MCI due to AD, and cognitively normal individuals. In an independent test set, the model achieved an area under the ROC curve of 96.2% for DLB classification. The investigators also examined spatial patterns contributing to model predictions, providing an initial link between computational classification and neurobiologically interpretable imaging patterns (Etminani et al., 2022).

These results are encouraging but require careful interpretation. The model was developed in a retrospective research setting using data derived from established cohorts. Performance in routine clinical populations, particularly among patients with atypical presentations or mixed pathology, may not generalise beyond the cohorts in which the model was developed. The ability to visualise the regions contributing to a prediction is nevertheless important. If a model consistently identifies brain regions compatible with established DLB metabolic patterns, this may increase confidence that it is learning biologically meaningful information. Conversely, unexpected areas of importance may indicate potential confounding or dataset-specific artefacts (Bruckert et al., 2020; Borchert et al., 2023).

3.3. Clinical and Neuropsychological Data

AI is not limited to imaging. Clinical variables may provide important information that is less expensive and more accessible than advanced imaging. The major advantage of combining such features is that individual clinical manifestations that have limited diagnostic specificity may become more informative when considered together.

However, models based on clinical features are highly dependent on the quality and completeness of clinical documentation. Symptoms may be inconsistently recorded, and the apparent absence of a symptom may reflect failure to document it rather than true absence (Bruckert et al., 2020; Goldfarb & Teodoridis, 2022).

4. Multimodal AI and Biomarker Integration

The increasing availability of molecular biomarkers creates an opportunity to move AI research beyond syndromic classification towards biological characterisation. α-Synuclein seed amplification assays are particularly important in this context. These methods detect seeding activity associated with pathological α-synuclein and may provide a more direct indication of synucleinopathy than conventional clinical biomarkers. Recent reviews and meta-analyses support their potential diagnostic value, while also highlighting methodological differences in substrates, replicates, positivity thresholds, and biological specimens (Kuang et al., 2024; Bregendahl et al., 2025).

Nevertheless, multimodal integration presents substantial methodological challenges. Different data types have different distributions, missing-data mechanisms, measurement errors, and acquisition standards. Large sample sizes are required to estimate interactions reliably. In small datasets, increasing the number of modalities may actually worsen model stability. Consequently, multimodal AI should not be interpreted as inherently superior to simpler models. The appropriate model complexity depends on dataset size, quality, structure, and clinical objective (Kelly et al., 2019; Acosta et al., 2022; Borchert et al., 2023).

5. AI for Early Detection and Prognosis

The potential value of AI in DLB extends beyond established dementia. Because Lewy body disease may become clinically apparent years before dementia, AI could contribute to identifying individuals at increased risk and characterising prodromal disease (McKeith et al., 2020). Prodromal manifestations may include RBD, autonomic dysfunction, hyposmia, subtle motor abnormalities, neuropsychiatric symptoms, and MCI-LB. However, individual clinical manifestations are not sufficiently specific to predict DLB in every patient. AI may provide a framework for integrating several weak or moderate predictors into a single individualised risk estimate (McKeith et al., 2020; Borchert et al., 2023).

Table 2 summarises clinical and biological studies that provide a foundation for future AI-based approaches to early detection and prognostic assessment in DLB. These studies illustrate the increasing importance of multimodal information, including neuroimaging, EEG, plasma biomarkers, α-synuclein-related biomarkers, and longitudinal clinical features. Importantly, the studies listed are not presented as validated AI or machine-learning models. Rather, they provide clinical and biological predictors that may serve as candidate inputs for future predictive models and help define relevant targets for AI-based prognostic assessment.

Table 2. Clinical and biological studies informing future AI-based early detection and prognostic modelling in DLB

Study	Population / data	Study type	Biomarker / approach	Outcome	Main finding
Postuma et al. (2019)	Isolated RBD	Non-AI longitudinal study	Longitudinal clinical assessment	Phenoconversion	RBD identifies individuals at substantial risk of future synucleinopathy
McKeith et al. (2020)	Prodromal DLB	Non-AI clinical criteria study	Clinical research criteria	Prodromal disease	Established MCI-LB and other prodromal presentations that can support early identification
Hasoon et al. (2026)	MCI-LB	Non-AI multimodal biomarker/prognostic study	MRI + EEG + plasma biomarkers + cognition	Dementia progression	Multimodal MRI, EEG, plasma biomarker, and cognitive measures improved prognostic assessment and may provide candidate features for future AI-based prognostic models
Barba et al. (2024)	Lewy body disease	Non-AI biomarker/clinical study	Amyloid/tau + clinical data	Cognitive outcome	AD co-pathology contributes to clinical heterogeneity and may be relevant to future biological stratification

5.1. REM Sleep Behaviour Disorder

Isolated RBD represents one of the strongest clinical markers of an underlying synucleinopathy. Longitudinal studies have demonstrated that a substantial proportion of individuals with idiopathic RBD eventually develop Parkinson's disease, DLB, or multiple system atrophy (Postuma et al., 2019).

The long latency between RBD and overt neurodegenerative disease creates an important potential window for prediction. However, RBD does not determine the final phenotype. Some patients develop predominantly parkinsonian disease, whereas others develop dementia or combined motor and cognitive manifestations. AI could integrate sleep characteristics with demographic, neurological, olfactory, autonomic, cognitive, imaging, and molecular information. Such an approach may also be relevant to disease-modifying trials, in which identification of biologically enriched individuals before substantial clinical deterioration could be important. However, long-term follow-up is essential. Short follow-up periods may classify individuals as non-converters simply because they have not yet developed clinically recognisable disease (Postuma et al., 2019; McKeith et al., 2020; Simuni et al., 2024).

5.2. Mild Cognitive Impairment with Lewy Bodies

MCI-LB represents another important population for predictive AI. Individuals already demonstrate measurable cognitive impairment but may not yet have progressed to established dementia. A particularly relevant 2026 study by Hasoon et al. investigated multimodal biomarkers in MCI-LB using MRI, EEG, plasma biomarkers, and cognitive assessment. In probable MCI-LB, smaller hippocampal and posterior cortical volumes were associated with shorter dementia-free survival, while EEG abnormalities and plasma biomarkers were also associated with progression. Importantly, combining biomarkers across modalities improved prognostic models compared with individual measurements alone (Hasoon et al., 2026). These findings do not establish a clinically validated AI system, but they provide an important biological rationale for multimodal prognostic modelling.

5.3. Prediction of Cognitive Decline

Prediction of cognitive decline is one of the most clinically relevant potential applications of AI in DLB. Cognitive decline in DLB shows substantial variability in its rate and pattern. AD co-pathology may contribute to this heterogeneity, with amyloid and tau pathology potentially associated with greater cognitive burden and different trajectories (Barba et al., 2024).

A prognostic model could incorporate baseline cognition, disease duration, motor severity, hallucinations, RBD, autonomic dysfunction, AD biomarkers, α-synuclein biomarkers, neuroimaging, and longitudinal changes. The advantage of AI lies in its ability to model interactions among predictors. However, a statistically significant association does not necessarily translate into clinically useful prediction (Steyerberg et al., 2010; Collins et al., 2015).

6. Explainable AI and Clinical Decision Support

A model may achieve excellent classification performance while relying partly on characteristics unrelated to disease biology. In neuroimaging, for example, an algorithm could inadvertently learn scanner-specific or centre-specific characteristics rather than disease-associated metabolic patterns. This is commonly referred to as the black-box problem (Bruckert et al., 2020; Borchert et al., 2023).

Explainable AI has therefore become an important component of clinical AI research. Explainability can improve transparency, facilitate model auditing, and help clinicians determine whether predictions are based on clinically plausible information (Amann et al., 2020; Ghassemi et al., 2021).

In neuroimaging, saliency maps and activation-based approaches can identify regions contributing to a model's prediction. In FDG-PET, for example, such methods may help determine whether computational models are focusing on regions compatible with known DLB-associated metabolic abnormalities. Feature-based models can use approaches such as permutation importance or local surrogate explanations to estimate the contribution of individual variables (Ribeiro et al., 2016; Lundberg & Lee, 2017).

7. Limitations and Challenges

DLB datasets are generally smaller than those available for AD. This creates a mismatch between the complexity of some algorithms and the number of available patients. When a model contains many parameters relative to the number of observations, it may learn dataset-specific characteristics rather than generalisable disease patterns. Cross-validation and regularisation can reduce overfitting but cannot compensate completely for inadequate sample size (Collins et al., 2015; Wolff et al., 2019; Borchert et al., 2023).

One of the most important weaknesses of current AI research is the limited use of independent external cohorts. A random train-test split within one dataset does not demonstrate generalisability to another hospital, geographic region, scanner, or clinical population. This is particularly important for neuroimaging because differences in scanners, acquisition parameters, preprocessing, reconstruction, and demographic characteristics can affect model predictions. The promising performance reported by individual imaging studies should therefore be interpreted within the context of their validation strategy (Etminani et al., 2022; Hefnawy et al., 2025).

A model developed in a specialised movement-disorders clinic may perform well in a population enriched for typical DLB but poorly in general practice. This is known as spectrum bias. It is particularly relevant to DLB because the intended clinical population is likely to include patients with early, atypical, and mixed presentations. If a model is trained using a clinical diagnosis that is itself incorrect in some individuals, the algorithm may learn to reproduce diagnostic errors. Biologically informed reference standards may improve this situation. α-synuclein seed amplification assays provide an important opportunity in this respect, although assay methodologies and clinical interpretation are still evolving (Bregendahl et al., 2025).

Mixed pathology remains one of the greatest challenges. A patient may have evidence of both α-synuclein and AD pathology. Binary classification may therefore be biologically inappropriate. Future systems should increasingly use multilabel or probabilistic approaches capable of representing concurrent pathological processes (Simuni et al., 2024).

Standardised reporting is required to improve reproducibility and facilitate meaningful comparisons. A model may demonstrate excellent discrimination but provide little additional value to clinicians. For example, distinguishing established DLB from healthy controls may be technically impressive but clinically less important than distinguishing DLB from AD in an ambiguous patient (Collins et al., 2015; Wolff et al., 2019).

Future studies should therefore assess whether AI improves diagnostic accuracy, time to diagnosis, biomarker utilisation, prognostic decisions, treatment selection, or patient outcomes. AI requires large datasets, creating important privacy and governance challenges. Bias may also arise if datasets do not adequately represent different demographic or clinical populations. Furthermore, AI systems may experience model drift as clinical practice, imaging technology, patient populations, and diagnostic criteria evolve. Clinical AI should therefore be regarded as a system requiring ongoing monitoring and recalibration rather than as a static algorithm (Kelly et al., 2019; Amann et al., 2020).

8. Future Perspectives

Recent evidence suggests that seed amplification assays can detect pathological α-synuclein with high diagnostic performance, although substantial methodological variation remains and performance may vary according to biological specimen and clinical comparison group (Simuni et

al., 2024). The limited size of individual DLB cohorts creates a strong rationale for multicentre collaboration (Borchert et al., 2023). Federated learning may allow algorithms to be trained across institutions without requiring all raw patient data to be transferred to a central location. This could increase dataset size and diversity while reducing some data-sharing barriers (Rieke et al., 2020).

A longer-term possibility is the use of AI to predict individual treatment response. Patients with DLB may respond differently to symptomatic therapies, and treatment effects may depend on the underlying biological phenotype (Simuni et al., 2024). AI could integrate clinical phenotype, biomarkers, imaging, and disease trajectory to estimate the probability of benefit from specific interventions. At present, however, evidence for AI-based individualised treatment selection in DLB remains limited, and this should be considered a research objective rather than an established application (Kelly et al., 2019; Borchert et al., 2023).

The future role of AI is unlikely to involve the complete replacement of neurologists. AI can process large datasets, detect subtle quantitative patterns, and generate standardised probabilistic estimates. Clinicians contribute contextual reasoning, recognition of atypical presentations, communication with patients and caregivers, ethical judgement, and consideration of individual preferences (Kelly et al., 2019; Amann et al., 2020).

9. A Proposed Framework for AI in DLB

Based on the current literature, the potential future role of AI in DLB can be conceptualised as a five-stage continuum describing the potential evolution of AI applications in DLB: early detection, diagnosis, biological stratification, prognostic and longitudinal assessment, and precision neurology (Figure 1). These stages were selected to reflect the main clinical questions that emerge across the disease continuum, from identifying individuals at increased risk to supporting increasingly individualized clinical decision-making. Importantly, the framework is intended as a conceptual roadmap rather than a representation of currently validated clinical applications.

Stage 1 – Early detection. The first stage involves identifying clinical and biological patterns associated with an increased risk of Lewy body disease before established dementia. Potential inputs include prodromal symptoms, longitudinal cognitive changes, neuroimaging, electrophysiological measures, and emerging biomarkers. Although individual risk markers are increasingly recognised, AI-based prediction of future DLB remains largely prospective. The potential advantage of AI at this stage is the integration of multiple weak or heterogeneous signals that may be difficult to interpret independently.

Stage 2 – Diagnosis. The second stage focuses on integrating clinical, imaging, electrophysiological, and biomarker information to support the diagnosis and differential diagnosis of DLB. This represents the most developed component of the proposed framework, with several studies demonstrating the feasibility of machine-learning approaches using MRI, FDG-PET, EEG, and multimodal data. However, differences in datasets, diagnostic standards, acquisition protocols, and external validation currently limit routine clinical implementation. Thus, AI should be considered a diagnostic support tool rather than a replacement for clinical assessment.

Stage 3 – Biological stratification. This stage extends AI applications beyond diagnostic classification toward characterising the biological heterogeneity of DLB. AI could potentially integrate information related to α-synuclein pathology, Alzheimer's disease co-pathology, neuroimaging, and other biomarkers to define biologically meaningful patient profiles. This application remains at an emerging stage and will depend on the continued development, standardisation, and validation of biological biomarkers. **Stage 4 – Prognostic and longitudinal assessment.** The fourth stage addresses the marked heterogeneity of DLB progression. By integrating repeated clinical assessments, imaging, electrophysiological measures, biomarkers, and potentially digital biomarkers, AI may support prediction of cognitive, motor, neuropsychiatric, and functional trajectories. Compared with diagnostic

applications, prognostic AI in DLB remains less mature and requires larger longitudinal datasets, external validation, and careful consideration of missing data, censoring, and competing risks.

Stage 5 – Precision neurology. The final stage represents the most prospective component of the framework. By combining diagnostic, biological, and prognostic information, AI could eventually support individualized monitoring, clinical-trial recruitment, and potentially treatment selection. At present, however, there is insufficient evidence to support AI-guided treatment selection in DLB. Therefore, precision neurology should be regarded as a future direction dependent on successful validation of the preceding stages.

This framework illustrates the conceptual shift:

AI-assisted diagnosis → AI-supported biological characterisation → AI-supported prognosis → AI-enabled precision neurology

The transition between these stages should be evidence-based. Each additional clinical application requires independent validation and demonstration of incremental clinical benefit.

Importantly, progression across these stages should be evidence-based. Increasing model complexity or predictive performance alone is insufficient to justify clinical implementation. Each new application requires independent validation, assessment of calibration and generalisability, interpretability where appropriate, and demonstration of incremental clinical utility. Accordingly, the proposed framework should be viewed as a developmental roadmap, with diagnostic applications currently having the strongest evidence, while biological stratification and prognostic applications remain emerging and precision neurology remains largely prospective.

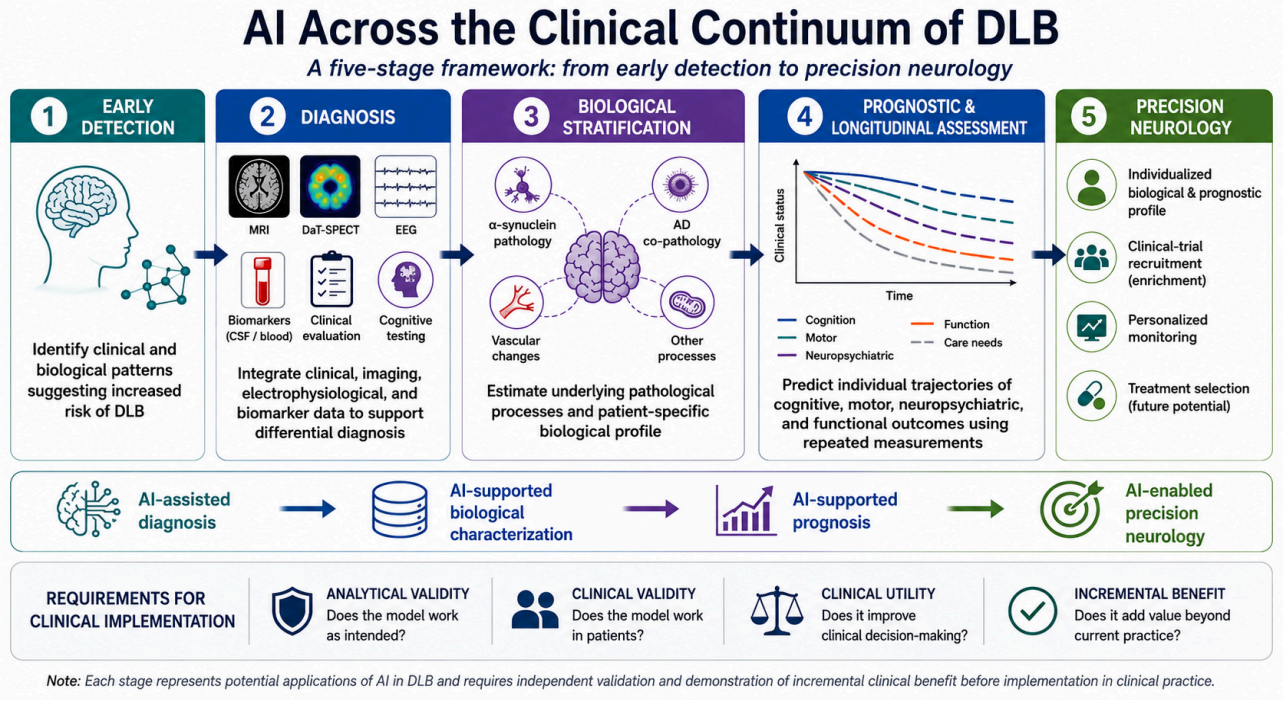

Figure 1. Proposed framework for AI in dementia with Lewy bodies (DLB). The framework depicts a five-stage continuum from early detection and diagnosis to biological stratification, prognostic assessment, and precision neurology. The progression reflects the potential evolution of AI from diagnostic support towards individualised prognostic and clinical applications. Each stage requires appropriate validation and evidence of clinical utility before implementation in practice. Created by the authors using Microsoft Copilot (AI-generated illustration), based on the conceptual framework proposed in this review.

10. Conclusions

AI is emerging as a potentially valuable component of research in dementia with Lewy bodies. Current studies demonstrate that machine-learning and deep-learning approaches can identify clinically relevant patterns in neuroimaging, clinical variables, and heterogeneous biomarker datasets. Importantly, some biomarkers discussed in this review have been investigated primarily using conventional approaches rather than AI or machine-learning methods; their potential value for future AI models therefore remains prospective. The potential value of AI extends beyond established diagnosis. Integration of clinical, imaging, molecular, EEG, and digital information may support prodromal risk prediction, biological stratification, prognosis, and longitudinal monitoring.

Nevertheless, the current evidence does not justify routine autonomous AI-based diagnosis. The major barriers to clinical implementation include limited dataset size and diversity, insufficient external and prospective validation, imperfect reference standards, mixed pathology, spectrum bias, and methodological heterogeneity.

The next phase of research should therefore prioritise large multicentre longitudinal datasets, biologically informed reference standards, standardised reporting, external validation, calibrated prediction, explainability, and prospective assessment of clinical utility.

References

Acosta, J. N., Falcone, G. J., Rajpurkar, P., & Topol, E. J. (2022). Multimodal biomedical AI. *Nature Medicine, 28*(9), 1773–1784. https://doi.org/10.1038/s41591-022-01981-2

Amann, J., Blasimme, A., Vayena, E., Frey, D., Madai, V. I., & Precise4Q Consortium. (2020). Explainability for artificial intelligence in healthcare: A multidisciplinary perspective. *BMC Medical Informatics and Decision Making, 20*(1), Article 310. https://doi.org/10.1186/s12911-020-01332-6

Baiardi, S., Hansson, O., Levin, J., & Parchi, P. (2024). In vivo detection of Alzheimer's and Lewy body disease concurrence: Clinical implications and future perspectives. *Alzheimer's & Dementia, 20*(8), 5757–5770. https://doi.org/10.1002/alz.14039

Barba, L., Abu-Rumeileh, S., Barthel, H., Massa, F., Foschi, M., Bellomo, G., Gaetani, L., Thal, D. R., Parnetti, L., & Otto, M. (2024). Clinical and diagnostic implications of Alzheimer's disease copathology in Lewy body disease. *Brain, 147*(10), 3325–3343. https://doi.org/10.1093/brain/awae203

Borchert, R. J., Azevedo, T., Badhwar, A. P., Bernal, J., Betts, M., Bruffaerts, R., Burkhart, M. C., Dewachter, I., Gellersen, H. M., Low, A., Lourida, I., Machado, L., Madan, C. R., Malpetti, M., Mejia, J., Michopoulou, S., Muñoz-Neira, C., Pepys, J., Peres, M., . . . Rittman, T. (2023). Artificial intelligence for diagnostic and prognostic neuroimaging in dementia: A systematic review. *Alzheimer's & Dementia, 19*(12), 5885–5904. https://doi.org/10.1002/alz.13412

Bregendahl, M., Kaya, Z. B., Singer, W., & McLean, P. J. (2025). Alpha-synuclein seeding amplification assays in Lewy body dementia: A brief review. *Molecular Neurodegeneration, 20*(1), Article 77. https://doi.org/10.1186/s13024-025-00868-3

Bruckert, S., Finzel, B., & Schmid, U. (2020). The next generation of medical decision support: A roadmap toward transparent expert companions. *Frontiers in Artificial Intelligence, 3*, Article 507973. https://doi.org/10.3389/frai.2020.507973

Collins, G. S., Reitsma, J. B., Altman, D. G., & Moons, K. G. (2015). Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement. *BMJ, 350*, Article g7594. https://doi.org/10.1136/bmj.g7594

Diab, R. A., Serag, I., Hassan, A., Azzam, A., Diab, M., Ali, M. A., Hefnawy, M. T., & Negida, A. (2025). Explainable AI models for detection of dementia with Lewy body: A scoping review (P5-3.003) [Abstract]. *Neurology, 104*(7, Suppl. 1), Article 1745. https://doi.org/10.1212/WNL.0000000000208720

Etminani, K., Soliman, A., Davidsson, A., Chang, J. R., Martínez-Sanchis, B., Byttner, S., Camacho, V., Bauckneht, M., Stegeran, R., Ressner, M., Agudelo-Cifuentes, M., Chincarini, A., Brendel, M., Rominger, A., Bruffaerts, R., Vandenberghe, R., Kramberger, M. G., Trost, M., Nicastro, N., . . . Ochoa-Figueroa, M. (2022). A 3D deep learning model to predict the diagnosis of dementia with Lewy bodies, Alzheimer's disease, and mild cognitive impairment using brain 18F-FDG PET. *European Journal of Nuclear Medicine and Molecular Imaging, 49*(2), 563–584. https://doi.org/10.1007/s00259-021-05483-0

Ghassemi, M., Oakden-Rayner, L., & Beam, A. L. (2021). The false hope of current approaches to explainable artificial intelligence in health care. *The Lancet Digital Health, 3*(11), e745–e750. https://doi.org/10.1016/S2589-7500(21)00208-9

Goldfarb, A., & Teodoridis, F. (2022, March 9). *Why is AI adoption in health care lagging?* Brookings Institution. https://www.brookings.edu/articles/why-is-ai-adoption-in-health-care-lagging/

Hasoon, J., Hamilton, C. A., Firbank, M., Schumacher, J., Colloby, S. J., Donaghy, P. C., Taylor, J.-P., & Thomas, A. J. (2026). Multimodal biomarkers to predict dementia-free survival and cognitive decline in mild cognitive impairment with Lewy bodies. *Parkinsonism & Related Disorders, 145*, Article 108265. https://doi.org/10.1016/j.parkreldis.2026.108265

Hefnawy, M. T., Serag, I., Azzam, A. Y., Ali, M. A., Hassan, A. K., Diab, R. A., Diab, M., & Negida, A. (2025). Role of combining artificial intelligence (AI) and neuroimaging in detecting dementia with Lewy bodies (DLB): A scoping review (P3-5.027) [Abstract]. *Neurology, 104*(7, Suppl. 1), Article 1740. https://doi.org/10.1212/WNL.0000000000208716

Kaya, Z. B., Amerna, D., Susarla, A., Lim, M. J., Bregendahl, M., Sekiya, H., DeTure, M., Ross, O. A., Dickson, D. W., Boschen, S. L., & McLean, P. J. (2026). Molecular profiling of alpha-synuclein pathology and seeding activity in Parkinson's disease. *Acta Neuropathologica, 151*(1), Article 54. https://doi.org/10.1007/s00401-026-03026-1

Kelly, C. J., Karthikesalingam, A., Suleyman, M., Corrado, G., & King, D. (2019). Key challenges for delivering clinical impact with artificial intelligence. *BMC Medicine, 17*(1), Article 195. https://doi.org/10.1186/s12916-019-1426-2

Kim, S., Jeon, S., Cho, K., Kang, S., Bang, S., Ye, B. S., & Lee, J. M. (2026). Deep learning for FDG-PET classification in patients with Alzheimer's disease, dementia with Lewy bodies and their mixed pathology: A solution for diagnostic heterogeneity. *Frontiers in Aging Neuroscience, 18*, Article 1780858. https://doi.org/10.3389/fnagi.2026.1780858

Kuang, Y., Mao, H., Huang, X., Chen, M., Dai, W., Gan, T., Wang, J., Sun, H., Lin, H., Liu, Q., Yang, X., & Xu, P. Y. (2024). α-Synuclein seeding amplification assays for diagnosing synucleinopathies: An innovative tool in clinical implementation. *Translational Neurodegeneration, 13*(1), Article 56. https://doi.org/10.1186/s40035-024-00449-2

Lundberg, S. M., & Lee, S.-I. (2017). A unified approach to interpreting model predictions. In I. Guyon, U. von Luxburg, S. Bengio, H. Wallach, R. Fergus, S. Vishwanathan, & R. Garnett (Eds.), *Advances in neural information processing systems* (Vol. 30, pp. 4765–4774). Curran Associates, Inc. https://proceedings.neurips.cc/paper/2017/hash/8a20a8621978632d76c43dfd28b67767-Abstract.html

McCombe, N., Joshi, A., Finn, D. P., McClean, P. L., Roberts, G., O'Brien, J. T., Thomas, A. J., Kane, J. P. M., & Wong-Lin, K. (2022). Distinguishing Lewy body dementia from Alzheimer's disease using machine learning on heterogeneous data: A feasibility study. In *2022 44th Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)* (pp. 4929–4933). IEEE. https://doi.org/10.1109/EMBC48229.2022.9871714

McKeith, I. G., Boeve, B. F., Dickson, D. W., Halliday, G., Taylor, J. P., Weintraub, D., Aarsland, D., Galvin, J., Attems, J., Ballard, C. G., Bayston, A., Beach, T. G., Blanc, F., Bohnen, N., Bonanni, L., Bras, J., Brundin, P., Burn, D., Chen-Plotkin, A., . . . Kosaka, K. (2017).

Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. *Neurology, 89*(1), 88–100. https://doi.org/10.1212/WNL.0000000000004058

McKeith, I. G., Ferman, T. J., Thomas, A. J., Blanc, F., Boeve, B. F., Fujishiro, H., Kantarci, K., Muscio, C., O'Brien, J. T., Postuma, R. B., Aarsland, D., Ballard, C., Bonanni, L., Donaghy, P., Emre, M., Galvin, J. E., Galasko, D., Goldman, J. G., Gomperts, S. N., . . . prodromal DLB Diagnostic Study Group. (2020). Research criteria for the diagnosis of prodromal dementia with Lewy bodies. *Neurology, 94*(17), 743–755. https://doi.org/10.1212/WNL.0000000000009323

Neupane, S., & Hortobágyi, T. (2025). Molecular crossroads: Shared and divergent molecular signatures in Alzheimer's disease and dementia with Lewy bodies. *International Journal of Molecular Sciences, 26*(24), Article 11811. https://doi.org/10.3390/ijms262411811

Postuma, R. B., Iranzo, A., Hu, M., Högl, B., Boeve, B. F., Manni, R., Oertel, W. H., Arnulf, I., Ferini-Strambi, L., Puligheddu, M., Antelmi, E., Cochen De Cock, V., Arnaldi, D., Mollenhauer, B., Videnovic, A., Sonka, K., Jung, K. Y., Kunz, D., Dauvilliers, Y., . . . Pelletier, A. (2019). Risk and predictors of dementia and parkinsonism in idiopathic REM sleep behaviour disorder: A multicentre study. *Brain, 142*(3), 744–759. https://doi.org/10.1093/brain/awz030

Ribeiro, M. T., Singh, S., & Guestrin, C. (2016). "Why should I trust you?": Explaining the predictions of any classifier. In *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining* (pp. 1135–1144). Association for Computing Machinery. https://doi.org/10.1145/2939672.2939778

Rieke, N., Hancox, J., Li, W., Milletarì, F., Roth, H. R., Albarqouni, S., Bakas, S., Galtier, M. N., Landman, B. A., Maier-Hein, K., Ourselin, S., Sheller, M., Summers, R. M., Trask, A., Xu, D., Baust, M., & Cardoso, M. J. (2020). The future of digital health with federated learning. *npj Digital Medicine, 3*, Article 119. https://doi.org/10.1038/s41746-020-00323-1

Simuni, T., Chahine, L. M., Poston, K., Brumm, M., Buracchio, T., Campbell, M., Chowdhury, S., Coffey, C., Concha-Marambio, L., Dam, T., DiBiaso, P., Foroud, T., Frasier, M., Gochanour, C., Jennings, D., Kieburtz, K., Kopil, C. M., Merchant, K., Mollenhauer, B., . . . Marek, K. (2024). A biological definition of neuronal α-synuclein disease: Towards an integrated staging system for research. *The Lancet Neurology, 23*(2), 178–190. https://doi.org/10.1016/S1474-4422(23)00405-2

Scott, G. D., Arnold, M. R., Beach, T. G., Gibbons, C. H., Kanthasamy, A. G., Lebovitz, R. M., Lemstra, A. W., Shaw, L. M., Teunissen, C. E., Zetterberg, H., Taylor, A. S., Graham, T. C., Boeve, B. F., Gomperts, S. N., Graff-Radford, N. R., Moussa, C., Poston, K. L., Rosenthal, L. S., Sabbagh, M. N., . . . Irwin, D. J. (2022). Fluid and tissue biomarkers of Lewy body dementia: Report of an LBDA symposium. *Frontiers in Neurology, 12*, Article 805135. https://doi.org/10.3389/fneur.2021.805135

Steyerberg, E. W., Vickers, A. J., Cook, N. R., Gerds, T., Gonen, M., Obuchowski, N., Pencina, M. J., & Kattan, M. W. (2010). Assessing the performance of prediction models: A framework for traditional and novel measures. *Epidemiology, 21*(1), 128–138. https://doi.org/10.1097/EDE.0b013e3181c30fb2

Wolff, R. F., Moons, K. G. M., Riley, R. D., Whiting, P. F., Westwood, M., Collins, G. S., Reitsma, J. B., Kleijnen, J., Mallett, S., & PROBAST Group. (2019). PROBAST: A tool to assess the risk of bias and applicability of prediction model studies. *Annals of Internal Medicine, 170*(1), 51–58. https://doi.org/10.7326/M18-1376