13th COGNITIVE DAY

9 MAY 2025, LJUBLJANA, SLOVENIA

Decoding Lewy Body Dementia:
Translating Scientific Discoveries into Clinical Advances

13th COGNITIVE DAY

Decoding Lewy Body Dementia: Translating Scientific Discoveries into Clinical Advances

Published by:
Centre for Cognitive Impairments, Department of Neurology, University Medical Centre Ljubljana

Date and place of publication:
2025, Ljubljana

Edited by:
Milica Gregorič Kramberger

Access to e-booklet:
Preceding was published only in e-version (format PDF) at 13th Cognitive Day meeting on 9 May 2025. It is available for download at: Slovenian Neurological Association, www.zdruzenjenevrologov.si

Cognitive Day is an annual scientific meeting with international participation organised by Centre for Cognitive Impairments, Department of Neurology, University Medical Centre Ljubljana.

Kataložni zapis o publikaciji (CIP) pripravili v Narodni in univerzitetni knjižnici v Ljubljani.

COBISS.SI-ID 235156739
ISBN 978-961-7080-11-7 (PDF)

Contents

List of speakers

Zvezdan PIRTOŠEK, MD, PhD
Professor of Neurology
Chair of Neurology
Medical Faculty University of Ljubljana
and Department of Neurology, University Medical Center
Ljubljana, Slovenia

Dag AARSLAND MD, PhD
Professor of Old Age Psychiatry
Director of the Centre for Healthy Brain Ageing,
Department of Psychological Medicine
and Head of the NIHR HealthTech Research Centre in Brain Health South London
and Maudsley NHS Foundation Trust, London, United Kingdom
and Director of research at Centre for Age Related Medicine, Stavanger University Hospital, Norway.

Tiago Fleming OUTEIRO, PhD
Professor of Aggregopathies,
Director of the Department of Experimental Neurodegeneration,
University Medical Center Göttingen, Göttingen, Germany

Andreja EMERŠIČ PhD, Eu SpLM
Laboratory for CSF diagnostics,
Neurology Clinic, University Medical Center, Ljubljana, Slovenia

Cene JERELE MD; PhD student
Consultant in Radiology
University Medical Center
Ljubljana, Slovenia
and Karolinska Institutet
Department of Neurobiology, Care Sciences and Society (NVS)
Division of Clinical Geriatrics
Huddinge, Sweden

Irena REKTOROVA, MD, PhD
Professor of Neurology
Head of the Movement Disorders Centre at the First Department of Neurology, School of Medicine and of the Applied Neuroscience Research Group at Central European Institute of Technology (CEITEC), Masaryk University in Brno, Czech Republic

Laura BONANNI, MD, PhD
Professor of Neurology
Head of Department of Medicine and Aging Sciences
Universita degli Studi ". dAnnunzio Chieti-Pescara, Italy

Maja TROŠT, MD, PhD
Professor of Neurology
Department of Neurology, University Medical Center Ljubljana
and Department of Nuclear Medicine, University Medical Center Ljubljana
and Medical Faculty University of Ljubljana, Slovenia

Preface

Dear colleagues,

It is a great pleasure to welcome you to the **13th Cognitive Day international meeting** and to present this selection of scientific articles and abstracts compiled for the occasion.

On behalf of the Organizing Committee, I am honored to introduce this year's meeting, which is dedicated to **Dementia with Lewy Bodies (DLB)** — a complex, multifaceted, and often underrecognized neurodegenerative disease.
DLB is recognized as the second most common cause of degenerative dementia after Alzheimer's disease. However, its diagnosis and management remain significant clinical challenges. Thanks to continuous research efforts and growing clinical awareness, we are increasingly better equipped to detect, understand, and manage this condition.

This meeting brings together leading international experts, clinicians, researchers, and healthcare professionals, united by a common goal: to share the latest advances, foster new collaborations, and advance innovation in the diagnosis and care of individuals affected by DLB.
We have prepared a comprehensive program designed to inspire meaningful discussions and provide valuable insights. This booklet contains essential information about the meeting, including the program schedule and abstracts.

Thank you for your participation and your dedication to improving the lives of individuals living with DLB and their families. A special thanks to all the speakers and contributors who made this meeting possible.
We wish you an engaging and fruitful experience.

Warm regards,
Associate Professor Milica Gregorič Kramberger, MD, PhD
Head of the Organizing Committee

Program

08:30 - 09:00 **Registration**

09:00 **Welcome and introduction**
Milica G. KRAMBERGER, Ljubljana, Slovenia

CLINICAL PRESENTATION

09:05 **Prodromal Dementia with Lewy bodies: What is it and how does it fit in the new neuronal synuclein disorder framework?**
Dag AARSLAND, Stavanger, Norway & London, UK

09:35 **Seeing the Invisible: Mechanisms of hallucinatory phenomena in Dementia with Lewy Bodies**
Zvezdan PIRTOŠEK, Ljubljana, Slovenia

10:05 - 10:15 **Discussion**

BIOMARKERS

10:15 **Understanding biology to classify and treat synucleinopathies**
Tiago Fleming OUTEIRO, Goettingen, Germany

10:45 **Identifying co-pathologies in Dementia with Lewy bodies: the role of fluid biomarkers**
Andreja EMERŠIČ, Ljubljana Slovenia

11:15 - 11:25 **Discussion**

11:25 - 11:45 **Coffee Break**

STRUCTURAL IMAGING

11:45 **Role of structural MRI in Dementia with Lewy Bodies**
Irena REKTOROVA, Brno, Czech Republic

12:15 **Cholinergic white matter and vascular pathology in Dementia with Lewy bodies: New insights from neuroimaging**
Cene JERELE, Ljubljana, Slovenia

12:45 - 12:55 **Discussion**

13:00 - 14:00 **LUNCH**

NEUROPHYSIOLOGY & FUNCTIONAL IMAGING

14:00 **The role of neurophysiology in diagnosis and treatment of Dementia with Lewy bodies**
Laura BONANNI, Chieti, Italy

14:30 **The role of molecular imaging in Dementia with Lewy bodies**
Maja TROŠT, Ljubljana, Sovenia

15:00 - 15:15 **Discussion**

15:15 **Closing remarks**

Prodromal Dementia with Lewy bodies: What is it and how does it fit in the new neuronal synuclein disorder framework?

Dag Aarsland

Like all the major neurodegenerative disorders, dementia with Lewy bodies (DLB) has an extended period of gradually increasing neuropathological changes before clinical symptoms emerge. The earliest pathological changes in DLB are alpha-synuclein accumulation, which usually starts in the brainstem and olfactory regions, leading to synaptic dysfunction, followed by spread to limbic and cortical areas. This pathology precedes the onset of full-blown cognitive and motor symptoms by years.
The prodromal stage of DLB is less well described compared to Alzheimer`s disease and Parkinson`s disease, but research criteria have been proposed (MCKetih et al 2020, 32661072). It is well established that REM sleep behavior disorder (RBD) is an early clinical indicator of subsequent DLB. Similarly, some patients with mild cognitive impairment (MCI), in particular those with non-amnestic MCI and one or more of the core DLB features (eg visual hallucinations, parkinsonism, fluctuating cognition, RBD), will develop DLB rather than Alzheimer`s disease.

The opportunity to reliably diagnose alpha-synucleinopathy in CSF has enabled the possibility to accurately diagnose DLB, and potentially also the prodromal and even the pre-clinical stages of DLB. This has led to the proposal of new biological classification systems for DLB and other alphasynuclein disorders, similar to that of Alzheimer`s disease (eg the ATN system). The neuronal synuclein disorder framework (Simuni T et al 2024) ,includes an integrated staging system (NSD-ISS).
This system is developed based on evidence in Parkinson`s disease.

In this lecture, I will discuss how it might fit with DLB, both manifest and prodromal DLB, and describe an ongoing research project aiming to assess this question.

Seeing the Invisible: Mechanisms of hallucinatory phenomena in Dementia with Lewy Bodies

Zvezdan Pirtošek

Abstract

Hallucinations — perceptions in the absence of external stimuli — represent one of the most striking and clinically significant symptoms in Dementia with Lewy Bodies (DLB). Among these, visual hallucinations (VHs) are particularly characteristic, often appearing early in the disease course, and serving as both a diagnostic hallmark and a window into deeper neural dysfunction. This lecture explores the multifactorial neurobiological, cognitive, and theoretical mechanisms underlying hallucinatory phenomena in DLB, integrating empirical findings with recent advances in systems neuroscience and consciousness studies.

Clinical and Phenomenological Overview

Dementia with Lewy Bodies is the second most common form of neurodegenerative dementia after Alzheimer's disease, defined by the accumulation of α-synuclein pathology in cortical and subcortical structures. Core clinical features include cognitive fluctuations, visual hallucinations, REM sleep behavior disorder (RBD), and parkinsonism.
Visual hallucinations affect up to 70–80% of patients and are typically well-formed, vivid, and recurrent, involving human figures, animals, or objects. Early in the disease, patients may retain insight into their hallucinatory experiences, which gradually diminishes as the disease progresses. Unlike hallucinations in psychotic disorders, those in DLB are less bizarre and often contextual. They are also strongly associated with caregiver burden, earlier institutionalization, and increased mortality risk.

Cognitive and Perceptual Mechanisms

Cognitive neuropsychology has revealed that hallucinations in DLB emerge from a disruption in the dynamic interaction between bottom-up sensory input and top-down cognitive control. Patients exhibit significant deficits in visuoperception, attention, and executive function, with poor contrast sensitivity, impaired figure-ground discrimination, and difficulty integrating visual information. These perceptual abnormalities create ambiguity, which the brain attempts to resolve — often by generating internally derived interpretations that manifest as hallucinations.
Cognitive fluctuations, a defining feature of DLB, further destabilize perceptual reality. Periods of reduced alertness, transient confusion, or dream-like mentation correlate temporally with hallucinatory episodes, suggesting that transient shifts in consciousness enable internally generated images to intrude into waking perception.

Structural and Functional Brain Correlates

Structural MRI studies consistently demonstrate occipital and parietal lobe atrophy in DLB, particularly in visual association areas. Hippocampal and temporal lobe involvement also contributes to impaired contextual memory and familiarity misattribution. Functional neuroimaging using FDG-PET and resting-state fMRI reveals occipital hypometabolism, disrupted dorsal attention networks, and increased activity in the default mode network (DMN) — all of which point to a breakdown in perceptual prediction and attentional control.
DLB is further characterized by reduced functional connectivity between frontal executive regions and posterior visual cortices. This results in diminished top-down correction of perceptual errors and facilitates the emergence of unfiltered or erroneous percepts. Emerging EEG studies reveal thalamo-cortical dysrhythmia and increased low-frequency oscillations, linking hallucinations to unstable cortical rhythms and impaired sensory gating.

Neurochemical Contributions

Neurochemical imbalances play a central role in DLB hallucinations. Severe cholinergic deficits, particularly in the occipital cortex, reduce the brain's capacity to filter visual noise and sustain attention. Dopaminergic dysregulation, while crucial for motor function, contributes to overactive salience attribution and hyperinterpretation of internal stimuli. This aligns DLB in part with psychotic models of hallucination, while maintaining its unique neurodegenerative profile.

Serotonergic and noradrenergic systems also modulate arousal and reality testing. Reduced serotonin receptor binding (especially 5-HT2A) in temporal and visual cortices may lower thresholds for hallucinatory intrusion. Pharmacological studies show that cholinesterase inhibitors (e.g., rivastigmine) can reduce hallucinations, while dopaminergic and anticholinergic medications often exacerbate them. Neuroleptic sensitivity remains a critical clinical issue, with typical antipsychotics potentially triggering severe, even fatal, reactions.

Theoretical Integration: Predictive Coding and Consciousness

Recent advances in cognitive neuroscience provide novel theoretical frameworks to understand hallucinations as active inferences rather than passive errors. According to the Bayesian brain hypothesis, perception results from hierarchical predictions generated by the brain, which are constantly updated against incoming sensory data. In DLB, degraded bottom-up input (due to visual processing deficits and cholinergic loss) leads the brain to rely more heavily on internal predictions or priors. When these priors dominate in the absence of reliable error correction, hallucinations occur.

This view aligns with Anil Seth's model of perception as "controlled hallucination." All perception, under this model, is a hallucinatory construction shaped by prior knowledge — constrained by sensory data. In DLB, these constraints weaken, resulting in "uncontrolled hallucinations" where top-down predictions become indistinguishable from reality. Visual hallucinations thus reveal the predictive nature of consciousness itself, distorted through neurodegeneration.

Evolutionary Perspective on Hallucinatory Phenomena

From an evolutionary standpoint, perception evolved to favor survival over veridical accuracy. A brain primed to detect potential threats — even at the risk of false positives — may have had adaptive value. Visual systems are evolutionarily ancient, and hallucinations may represent a reversion to more primitive, less supervised forms of perception. As the evolutionarily newer cortical regions (parietal, occipital, prefrontal) deteriorate in DLB, subcortical and limbic systems gain relative dominance, producing vivid percepts without contextual filtering. In this light, hallucinations may be understood as evolutionarily "disinhibited survival heuristics" emerging in the absence of modern neural governance.

Practical Implications and Clinical Strategies

Clinically, hallucinations in DLB are more than perceptual curiosities — they signal a more rapid cognitive decline and greater disease severity. Their management requires nuanced, interdisciplinary approaches. Non-pharmacological interventions should be prioritized, including reassurance, environmental adaptation (lighting, visual cues), and caregiver education. Medication review is essential, particularly for anticholinergic or dopaminergic agents.

Cholinesterase inhibitors remain the mainstay of pharmacological treatment. When antipsychotic medication becomes necessary, quetiapine may be used cautiously, while clozapine remains an alternative under specialist supervision. Pimavanserin, a 5-HT2A inverse agonist, holds promise in preliminary studies but is not widely available in all regions.

Emerging research into biomarkers — including occipital hypometabolism, EEG slowing, and neurotransmitter imaging — may enable earlier identification of hallucination-prone individuals and personalized therapeutic interventions.

Conclusion

Hallucinations in DLB arise from a complex interplay of sensory degradation, cognitive instability, network dysfunction, and neurochemical imbalance. They reflect the breakdown of systems responsible for integrating, predicting, and correcting perceptual input — ultimately revealing how the brain constructs reality. As such, they are not merely pathological, but epistemologically and neurologically revealing. By "seeing the invisible," both literally and conceptually, we gain insight into the architecture of consciousness, the vulnerability of perception, and the necessity of interdisciplinary research. Hallucinations in DLB offer a unique opportunity to bridge clinical neurology with theoretical neuroscience — and to advance both our science and our compassion.

REFERENCES

McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. 2017;89(1):88–100.

Aarsland D, Ballard C, Halliday G. Are Parkinson's disease with dementia and dementia with Lewy bodies the same entity? Lancet Neurol. 2021;20(5):301–311.

Shimizu S, Hanyu H, Asano T, et al. Differentiation of dementia with Lewy bodies from Alzheimer's disease using brain SPECT. Dement Geriatr Cogn Disord. 2005;20(1):25–30.

Peraza LR, Taylor JP, Kaiser M. Divergent brain functional network alterations in dementia with Lewy bodies and Alzheimer's disease. Neurobiol Aging. 2015;36(9):2458–2467.

Ballard C, Grace J, McKeith I, et al. Neuroleptic sensitivity in dementia with Lewy bodies and Alzheimer's disease. Lancet. 1998;351(9108):1032–1033.

McKeith I, Fairbairn A, Perry R, et al. Neuroleptic sensitivity in patients with senile dementia of Lewy body type. BMJ. 1994;308(6920):202–203.

Sawada H, Oeda T, Umemura A, et al. Cholinesterase inhibitors may reduce hallucinations in dementia with Lewy bodies. Int J Geriatr Psychiatry. 2019;34(4):522–528.

Friston K. A theory of cortical responses. Philos Trans R Soc Lond B Biol Sci. 2005;360(1456):815–836.

Adams RA, Stephan KE, Brown HR, Frith CD, Friston KJ. The computational anatomy of psychosis. Front Psychiatry. 2013;4:47.

Collerton D, Perry E, McKeith I. Why people see things that are not there: a novel perception and attention deficit model for recurrent complex visual hallucinations. Behav Brain Sci. 2005;28(6):737–757.

Seth AK. Being You: A New Science of Consciousness. London: Faber & Faber; 2021.

Seth AK. A predictive processing theory of sensorimotor contingencies: Explaining the puzzle of perceptual presence and its absence in synesthesia. Cogn Neurosci. 2014;5(2):97–118.

Barrett LF. How Emotions Are Made: The Secret Life of the Brain. Boston: Houghton Mifflin Harcourt; 2017.

Pessoa L. The Cognitive-Emotional Brain: From Interactions to Integration. Cambridge: MIT Press; 2013.

Understanding biology to classify and treat synucleinopathies

Tiago Fleming Outeiro

The molecular process of protein aggregation has been extensively studied in vitro over the years. However, the mechanisms governing protein folding and unfolding in the crowded cellular environment — where concentrations of proteins and other biomolecules are extremely high—remain less understood. This understanding is highly relevant not only in the context of normal biology, but also in the context of a variety of human conditions, ranging from cancer, to diabetes, and neurodegenerative disorders.

Cells must tightly regulate protein production, folding, clearance, and disaggregation in order to maintain protein homeostasis, or proteostasis [1]. This includes ensuring proper folding in diverse subcellular compartments and detecting and addressing instances of protein misfolding. The cellular proteostasis network encompasses molecular chaperones, degradation pathways such as the ubiquitin-proteasome system, and autophagy (Gidalevitz et al., 2010). This network also integrates signaling pathways that allow cells to respond to environmental perturbations that disrupt proteostasis, thereby mitigating damage and preventing cellular toxicity.

By targeting the molecular triggers of protein misfolding, it may be possible to interfere with the progression of protein aggregation at its earliest stages. Therefore, developing biomarkers capable of detecting these preclinical molecular changes would also enable early intervention, providing a promising avenue for the discovery of disease-modifying therapies (DMTs).
Under various conditions, including environmental stressors, genetic mutations, post-translational modifications, or simply the aging process, the proteostasis network may fail. This can lead to protein misfolding and the adoption of aberrant conformations, initiating aggregation processes. Some of the resulting aggregated species are thought to be cytotoxic, leading to neuronal dysfunction and death in neurodegenerative diseases.

Protein aggregation is a common feature in various neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), and rarer conditions such as prion diseases, all of which have devastating consequences for the brain. A shared hallmark of neurodegenerative diseases, beyond region-specific neuronal death, is the accumulation of protein aggregates in the brain, and in some cases, even in peripheral tissues. However, it is now widely accepted that protein pathology in the various neurodegenerative diseases is more complex than initially thought and that multiple pathologies/co-pathologies can occur [2], especially with aging. This understanding has strong implications for diagnosis and may prove useful also for disease classification.

In PD, dementia with Lewy bodies (DLB), pure autonomic failure (PAF) and multiple system atrophy (MSA), collectively referred to as synucleinopathies, α-synuclein (aSyn) is the key aggregating protein. Its misfolding and subsequent aggregation into oligomeric and fibrillar species represent central pathogenic events. These aggregates not only disrupt cellular functions but also contribute to the progressive neuronal loss observed in this disorder. Understanding how aSyn misfolds, aggregates, and interacts with the proteostasis network is therefore critical for developing effective therapeutic strategies to combat PD and related synucleinopathies.

PD is understood as a highly complex disorder. While the motor symptoms are the hallmark leading to diagnosis, prodromal phases exhibit signs such as hyposmia, REM sleep disturbances, gastrointestinal and behavioral changes. These early symptoms implicate multiple brain regions and even peripheral organs, such as the gut, before involvement of the dopaminergic substantia nigra. This region of the brain experiences extensive neuronal loss in PD, with the resulting dopamine deficiency contributing to the motor deficits characteristic of the disease.

Advances in understanding of genetic factors, environmental factors, and factors contributing to neurodegeneration suggest that PD should not be considered a singular homogeneous condition but rather a complex multifaceted group of related disorders arising due to the combination of various complex components (i.e. 'Parkinson's diseases'). Importantly, various pathophysiological mechanisms have been associated with PD and they are likely preferentially associated with specific factors. Consequently, there is an increasing need for a broad set of criteria to

classify and define PD based on biological markers rather than relying solely on descriptive, often subjective, clinical criteria.

The development of seeding amplification assays (SAA) has emerged as a powerful tool for detecting the presence of misfolded and aggregated proteins associated with neurodegenerative diseases [3-5]. These assays exploit the ability of pathological protein aggregates to induce the misfolding of their soluble monomeric counterparts, amplifying even minute amounts of disease-related species for detection. SAAs, such as Real-Time Quaking-Induced Conversion (RT-QuIC) and Protein Misfolding Cyclic Amplification (PMCA), have demonstrated remarkable sensitivity and specificity in identifying disease-associated aggregates in various biological samples, including cerebrospinal fluid, blood, and even skin biopsies [3, 4, 6, 7]. Recent studies further highlight the potential of these techniques to advance the understanding of disease heterogeneity and identify reliable biomarkers for early diagnosis [8, 9].

Several groups of international leaders have proposed classification systems neurodegenerative diseases, beginning with AD [10, 11] and most recently including PD. These PD-related proposals, initially designed for research purposes, are meant to serve as a foundation for diagnosis and differentiation between distinct PD subtypes [12-14]. As new biomarkers become available, these classification systems will continue to evolve and it is likely, and desirable, they become integrated in routine clinical practice.

In summary, the scientific community has made tremendous progress in our understanding of molecular mechanisms involved in neurodegenerative diseases. While laboratory models are essential for testing basic molecular mechanisms, it has also become evident that we need to use and develop more complex models that aim to recapitulate the genetic and cellular context of cells in the complex environment of the human brain. In turn, this requires the development of disease classification systems that capture the underlying biology/pathobiology so that we can attempt to recapitulate disease in model systems. Ultimately, the hope is that we can diagnose diseases early to maximize our chances of therapeutic success.

REFERENCES

1. Balch, W.E., et al., Adapting proteostasis for disease intervention. Science, 2008. 319(5865): p. 916-9.

2. Spires-Jones, T.L., J. Attems, and D.R. Thal, Interactions of pathological proteins in neurodegenerative diseases. Acta Neuropathol, 2017. 134(2): p. 187-205.

3. Frey, B., et al., Tau seed amplification assay reveals relationship between seeding and pathological forms of tau in Alzheimer's disease brain. Acta Neuropathol Commun, 2023. 11(1): p. 181.

4. Huang, J., et al., Pathological alpha-synuclein detected by real-time quaking-induced conversion in synucleinopathies. Exp Gerontol, 2024. 187: p. 112366.

5. Vascellari, S., C.D. Orru, and B. Caughey, Real-Time Quaking- Induced Conversion Assays for Prion Diseases, Synucleinopathies, and Tauopathies. Front Aging Neurosci, 2022. 14: p. 853050.

6. Concha-Marambio, L., et al., Seed amplification assay for the detection of pathologic alpha-synuclein aggregates in cerebrospinal fluid. Nat Protoc, 2023. 18(4): p. 1179-1196.

7. Vivacqua, G., et al., Salivary alpha-Synuclein RT-QuIC Correlates with Disease Severity in de novo Parkinson's Disease. Mov Disord, 2023. 38(1): p. 153-155.

8. Coysh, T. and S. Mead, The Future of Seed Amplification Assays and Clinical Trials. Front Aging Neurosci, 2022. 14: p. 872629.

9. Mok, T.H., et al., Seed amplification and neurodegeneration marker trajectories in individuals at risk of prion disease. Brain, 2023. 146(6): p. 2570-2583.

10. Jack, C.R., Jr., et al., Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimers Dement, 2024. 20(8): p. 5143-5169.

11. Jack, C.R., Jr., et al., A/T/N: An unbiased descriptive classification scheme for Alzheimer disease biomarkers. Neurology, 2016. 87(5): p. 539-47.

12. Hoglinger, G.U., et al., A biological classification of Parkinson's disease: the SynNeurGe research diagnostic criteria. Lancet Neurol, 2024. 23(2): p. 191-204.

13. Lang, A.E., et al., Initial biological classification of Lewy body diseases: No consensus on terminology. Alzheimers Dement, 2024.

14. Simuni, T., et al., A biological definition of neuronal alpha-synuclein disease: towards an integrated staging system for research. Lancet Neurol, 2024. 23(2): p. 178-190.

Identifying co-pathologies in Dementia with Lewy bodies: the role of fluid biomarkers

Andreja Emeršič

Most patients with neurodegenerative dementia receive only one diagnosis during life; however, more than half exhibit multiple pathologies at autopsy that likely contributed to their clinical presentation, rate of cognitive decline, and mortality (1–3). Because current evidence is largely derived from retrospective neuropathological data, our understanding of the impact of concomitant pathologies in dementia with Lewy bodies (DLB) is still limited. Cerebrospinal fluid (CSF) or blood-based biomarkers that reflect underlying co-pathologies may inform the prediction of disease progression and improve clinical trial design in the future (1,4).

DLB, the second most common neurodegenerative dementia, is characterized by the intracellular accumulation of α-synuclein aggregates in the form of Lewy bodies and Lewy neurites (5,6). Neuropathological studies have demonstrated a high prevalence of concomitant Alzheimer's disease (AD), TAR DNA-binding protein 43 (TDP-43), and cerebrovascular pathology in DLB (1). Intermediate or high levels of AD neuropathology, reported in up to 50% of patients with autopsy-confirmed Lewy body disease, have been associated with greater α-synuclein burden and worse prognosis (1,4). Poorer performance in memory tests, more rapid attention decline, and shorter life expectancy have been reported in DLB individuals with AD neuropathologic change or AD CSF biomarker profile compared to patients with Lewy body pathology alone (1,2,7,8). Furthermore, amyloidosis (decreased CSF Aβ42/40 ratio) and AD CSF profile which were more common among the patients with Lewy body disease and dementia (71% and 43%, respectively) compared to those at mild cognitive impairment stage (48% and 9%, respectively), suggest the frequency of AD co-pathology in DLB increases with the severity of cognitive impairment (2).

Corroborating previous findings, we observed decreased CSF Aβ42/40 ratio in 49%, and the A+T+ profile (decreased CSF Aβ42/40 ratio with increased phosphorylated tau (p-tau)) in 34% of our patients with probable DLB; CSF profile consistent with underlying amyloid or AD co-pathology in DLB was associated with poorer performance on mini-mental state examination (MMSE). Since newly developed blood-based biomarkers offer promising, less invasive tools for early and accurate AD diagnosis, we further evaluated plasma p-tau217 and brain-derived tau performance in our memory clinic cohort. Brain-derived tau and p-tau217 correlated with CSF Aβ42/40 ratio, total tau, and CSF p-tau181 and detected amyloid co-pathology in DLB with 73% and 83% accuracy, respectively. Similarly, higher plasma p-tau181 and p-tau231 concentrations were found in European-DLB Consortium cohort participants with abnormal CSF Aβ42 levels and associated with lower baseline MMSE scores and more rapid MMSE decline over time in this multicentric study (9).

Contrary to AD, the impact of coexistent TDP-43 proteinopathy in DLB is less investigated because we lack reliable biomarkers to identify pathological TDP-43 aggregation during life (1). The real-time quaking-induced conversion technique has been adapted to CSF TDP-43 protein but not studied in DLB (10). Nevertheless, neuropathological studies have shown that TDP-43 pathology is associated with greater Lewy pathology burden, occurs more frequently in the presence of concomitant AD, and might reduce the likelihood of a clinical DLB diagnosis (1,11–13).
To conclude, comorbid proteinopathies are prevalent and likely affect clinical presentation and disease progression in DLB. Combined assessment of α-synuclein disease-specific biomarkers and biomarkers of concomitant pathologies could facilitate early, accurate diagnosis and guide potential treatment approaches.

REFERENCES

1. Toledo JB, Abdelnour C, Weil RS, Ferreira D, Rodriguez-Porcel F, Pilotto A, et al. Dementia with Lewy bodies: Impact of co-pathologies and implications for clinical trial design. Alzheimer's Dement. 2023;19(1):318–32.

2. Plastini MJ, Abdelnour C, Young CB, Wilson EN, Shahid-Besanti M, Lamoureux J, et al. Multiple biomarkers improve diagnostic accuracy across Lewy body and Alzheimer's disease spectra. Ann Clin Transl Neurol. 2024;11(5):1197–210.

3. Robinson JL, Lee EB, Xie SX, Rennert L, Suh E, Bredenberg C, et al. Neurodegenerative disease concomitant proteinopathies are prevalent, age-related and APOE4-associated. Brain. 2018;141(7):2181–93.

4. Irwin DJ, Grossman M, Weintraub D, Hurtig HI, Duda JE, Xie SX, et al. Neuropathological and genetic correlates of survival and dementia onset in synucleinopathies: a retrospective analysis. Lancet Neurol. 2017;16(1):55.

5. Outeiro TF, Koss DJ, Erskine D, Walker L, Kurzawa-Akanbi M, Burn D, et al. Dementia with Lewy bodies: An update and outlook. Mol Neurodegener. 2019;14(1):1–18.

6. McKeith IG, Ferman TJ, Thomas AJ, Blanc F, Boeve BF, Fujishiro H, et al. Research criteria for the diagnosis of prodromal dementia with Lewy bodies. Neurology. 2020;94(17):743–55.

7. Ryman SG, Yutsis M, Tian L, Henderson VW, Montine TJ, Salmon DP, et al. Cognition at Each stage of lewy body disease with co-occurring Alzheimer's disease pathology. J Alzheimer's Dis. 2021;80(3):1243–56.

8. Andersson M, Zetterberg H, Minthon L, Blennow K, Londos E. The cognitive profile and CSF biomarkers in dementia with Lewy bodies and Parkinson's disease dementia. Int J Geriatr Psychiatry. 2011;26(1):100–5.

9. Gonzalez MC, Ashton NJ, Gomes BF, Tovar-Rios DA, Blanc F, Karikari TK, et al. Association of Plasma p-tau181 and p-tau231 Concentrations with Cognitive Decline in Patients with Probable Dementia with Lewy Bodies. JAMA Neurol. 2022;79(1):32–7.

10. Scialò C, Tran TH, Salzano G, Novi G, Caponnetto C, Chiò A, et al. TDP-43 real-Time quaking induced conversion reaction optimization and detection of seeding activity in CSF of amyotrophic lateral sclerosis and frontotemporal dementia patients. Brain Commun. 2020;2(2):1–14.

11. Buciuc M, Whitwell JL, Boeve BF, Ferman TJ, Graff-radford J, Savica R, et al. TDP-43 is associated with a reduced likelihood of rendering a clinical diagnosis of dementia with Lewy bodies in autopsy- confirmed cases of transitional/diffuse Lewy body disease. J Neurol. 2020;267(5):1444–53.

12. Nakashima-Yasuda H, Uryu K, Robinson J, Xie SX, Hurtig H, Duda JE, et al. Co-morbidity of TDP-43 proteinopathy in Lewy body related diseases. Acta Neuropathol. 2007;114(3):221–9.

13. McAleese KE, Walker L, Erskine D, Thomas AJ, McKeith IG, Attems J. TDP-43 pathology in Alzheimer's disease, dementia with Lewy bodies and ageing. Brain Pathol. 2017;27(4):472–9.

Role of structural MRI in Dementia with Lewy Bodies

Irena Rektorova

Based on biological definition of neuronal α-synuclein diseases (Simuni et al., 2024) or on SynNeurGe classification of Parkinson's disease (Höglinger et al., 2024), imaging will be utilized particularly for evaluating neurodegeneration. So far, dopaminergic imaging using PET or SPECT and cardiac scintigraphy has been particularly implicated for diagnostic purposes in dementia with Lewy bodies (DLB) (McKeith et al., 2017). However, MRI has a great potential to serve as a suitable, relatively cheap, non-invasive and widely available marker for detection of specific degeneration patterns for DLB subtyping and stratification, for assessing microstructural changes, evaluating loss of dopaminergic, cholinergic and noradrenergic neurons and integrity of particularly cholinergic and dopaminergic pathways, and for screening for potential comorbidities. Longitudinal MRI studies enable its use not only for diagnostic purposes but also for monitoring disease progression and potential treatment effects.

Structural MRI alterations

While earlier studies particularly pointed out atrophy and cortical thinning of insula, anterior cingulate and medial frontal structures in early prodromal DLB subjects (Blanc et al. 2015, Roquet et al., 2017), later studies describe specific DLB patterns of early atrophy containing rather occipital and posterior temporal cortices (Cohen et al. 2025, Wang D, 2024, Galli et al. 2023). Atrophy patterns may differ between males and females (Oltra et al., 2023). Various DLB subtypes were reported using cluster analysis based on demographic and clinical data, Alzheimer's disease (AD) and cerebrovascular biomarkers at baseline, and cognitive decline over 3 years of follow up (Inguanzo et al., 2023). The clusters included an older subtype with reduced cortical grey matter (GM) volumes, worse cognition, and faster cognitive decline, a subtype with low GM volumes in fronto-occipital regions, and a subtype of younger patients with the highest cortical GM volumes, proportionally lower GM volumes in basal ganglia and the highest frequency of cognitive fluctuations. A specific brain-clinical signature which predicted conversion to fully developed DLB over 4 years was described in patients with isolated REM sleep behavioural disorder (iRBD) using partial least squares between brain deformation and 27 clinical variables (Rahayel et al., 2021). The pattern consisted of deformation of both cortical and subcortical regions, including mainly the basal ganglia, thalamus, corona radiata, amygdala, frontal and temporal lobes, and cerebellum, while expansion was additionally described in the ventricular system and subarachnoid cisterns. The deformation score predicted conversion to DLB with odds ratio = 4.7.

Many authors explored atrophy in specific brainstem structures and basal forebrain to evaluate losses of dopaminergic, noradrenergic and cholinergic neurons and pathways. Nucleus basalis of Meynert (NBM) volume has been consistently reduced in cognitively impaired patients with Parkinson's disease (PD) and it was shown utility as a prognostic indicator of future cognitive decline (Slater et al., 2024). Atrophy of the NBM was repeatedly reported also in DLB patients and in early prodromal DLB (Schumacher et al., 2021, Woo K et al. 2025), while the mean functional connectivity from the nucleus to occipital cortex was increased (Schumacher et al., 2021). Similar functional compensatory mechanisms have been described from the basal ganglia structures to lateral temporal cortices in patients with mild cognitive impairment with Lewy bodies (MCI-LB) (Novakova et al., 2024), i.e. a prodromal, pre-dementia stage of DLB. While NBM atrophy was describe in both prodromal and fully blown DLB, based on longitudinal examination, GM atrophy progressed in regions with significant cholinergic innervation, with widespread and accelerated rates of atrophy in patients who progress to probable DLB (Kantarci et al., 2022).

Loss of dopaminergic neurons in substantia nigra pars compacta (SNc) and noradrenergic neurons in locus coeruleus (LC) have been studied using neuromelanin sensitive (NMS) MRI. It is a T1 fast spin echo sequence. Both dopaminergic neurons and noradrenergic neurons contain a pigment neuromelanin (NM). Source of the NM contrast is NM bind to iron which is paramagnetic. Therefore, NM signal is decreased in patients with DLB, already in early prodromal stages of the disease and in iRBD, particularly in the LC (Železníková et al. 2025, Ehrminger et al. 2016). Iron sensitive susceptibility weighted imaging (SWI) or T2* relaxometry can be used to visualize dorsal nigral hyperintensity (so-called swallow tail sign) in individual healthy subjects. It evaluates nigrosome-1 as an ovoid hyperintense region in the dorsolateral part of

the SNc (Theis et al. 2024). Decreased or loss of the signal is present in already 2/3 of iRBD patients (De Marzi et al. 2016). Although it is easy to evaluate, it provides only a qualitative assessment. Based on a systematic review and meta-analysis (Tseriotis et al. 2024), 3T MRI scans showed pooled sensitivity and specificity of 82% to distinguish DLB patients from healthy controls and other types of degenerative dementias. The authors concluded that loss of the swallow tail sign (STS) may thus serve as a supportive marker for diagnostic purposes. Another recent review demonstrated that diagnostic accuracy of STS loss for DLB differentiation from other dementias was 76–90% (Tseriotis et al. 2025). More precise quantitative susceptibility mapping uses a multi-echo GRE sequence to map iron deposition in SNs and other subcortical and cortical regions (Theis et al. 2024). The trend of increasing susceptibility in SNc from controls to iRBD and MCI-LB, and to DLB suggests that iron deposition in the substantia nigra starts to increase as early as the prodromal stage in DLB and continues to increase as the disease progresses, independent of parkinsonism severity (Chen et al. 2021). Postmortem data suggest that QSM values are associated with both glial density and tau burden (Wang et al. 2023). However, challenges remain in standardizing QSM processing algorithms to ensure consistent results across different studies.

Microstructural changes assessed by MRI using free water imaging

Free water imaging uses a bi-tensor diffusion model to assess early microstructural changes, i.e. increased free water in the posterior parts of the SNc in Parkinson's disease and early DLB stages (Ofori et al. 2017, Burciu et al. 2017). Further alterations can be observed with the disease progression in additional regions including insula, amygdala, posterior cingulum, parahippocampal, entorhinal, supramarginal, fusiform, retrosplenial and Rolandic operculum regions over 12 months (Chiu et al. 2024). Free water was increased in the cholinergic NBM in both DLB and AD. However, free water along the pedunculopontine-thalamus tract was increased only in DLB and related to visual hallucinations (Schumacher et al. 2023).

Screening LBD co-pathologies

While mesial temporal lobe atrophy is rare in pure DLB and intact hippocampi may serve as a supportive feature to distinguish DLB from AD (McKeith et al. 2017), atrophy of the hippocampus or distinct hippocampal subfields is present in coexisting AD-related co-pathology (Ye et al. 2024, Sakurai et al. 2025) which is present in up to 80% of all developed DLB subjects.

Other comorbidities may co-exist in DLB, and cerebrovascular changes manifested as high white matter hyperintensities () loads were reported to be present in 43% (more than 300 DLB cases evaluated). The WMH were associated with medial temporal atrophy, however, this association lost its significance when β-amyloid was included in the model (Rennie et al. 2024).

Acknowledgement:

Supported by EU Joint Program-Neurodegenerative Disease (JPND) project entitled "TACKLing the Challenges of PREsymptomatic Sporadic Dementia (TACKL-PRED)," project number 8F22005, and by National Institute for Neurology Research (Programme EXCELES, ID Project No. LX22NPO5107, Funded by the European Union – Next Generation EU).

REFERENCES

Simuni T, Chahine LM, Poston K, et al. A biological definition of neuronal α-synuclein disease: towards an integrated staging system for research. Lancet Neurol. 2024 Feb;23(2):178-190. doi: 10.1016/S1474-4422(23)00405-2.

Höglinger GU, Adler CH, Berg D, et al. A biological classification of Parkinson's disease: the SynNeurGe research diagnostic criteria. Lancet Neurol. 2024 Feb;23(2):191-204. doi: 10.1016/S1474-4422(23)00404-0.

McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. 2017 Jul 4;89(1):88-100. doi: 10.1212/WNL.0000000000004058.

Blanc F, Colloby SJ, Philippi N, et al. Cortical Thickness in Dementia with Lewy Bodies and Alzheimer's Disease: A Comparison of Prodromal and Dementia Stages. PLoS One. 2015 Jun 10;10(6):e0127396. doi: 10.1371/journal.pone.0127396.

Roquet D, Noblet V, Anthony P, Philippi N, Demuynck C, Cretin B, Martin-Hunyadi C, Loureiro de Sousa P, Blanc F. Insular atrophy at the prodromal stage of dementia with Lewy bodies: a VBM DARTEL study. Sci Rep. 2017 Aug 25;7(1):9437. doi: 10.1038/s41598-017-08667-7.

Cohen JS, Phillips J, Das SR, et al. Posterior hippocampal sparing in Lewy body disorders with Alzheimer's copathology: An in vivo MRI study. Neuroimage Clin. 2025;45:103714. doi: 10.1016/j.nicl.2024.103714.

Wang D, Honnorat N, Toledo JB, et al. Deep learning reveals pathology-confirmed neuroimaging signatures in Alzheimer's, vascular and Lewy body dementias. Brain. 2024 Dec 9:awae388. doi: 10.1093/brain/awae388.

Galli A, Pilotto A, Chiarini B, et al. Occipital atrophy signature in prodromal Lewy bodies disease. Alzheimers Dement (Amst). 2023 Nov 23;15(4):e12462. doi: 10.1002/dad2.12462.

Oltra J, Habich A, Schwarz CG, et al. Sex differences in brain atrophy in dementia with Lewy bodies. Alzheimers Dement. 2024 Mar;20(3):1815-1826. doi: 10.1002/alz.13571.

Inguanzo A, Mohanty R, Poulakis K, et al. NPJ Parkinsons Dis. 2024 Aug 16;10(1):159. doi: 10.1038/s41531-024-00759-2. PMID: 39152153; PMCID: PMC11329719.

Rahayel S, Postuma RB, Montplaisir J, et al. A Prodromal Brain-Clinical Pattern of Cognition in Synucleinopathies. Ann Neurol. 2021 Feb;89(2):341-357. doi: 10.1002/ana.25962.

Slater NM, Melzer TR, Myall DJ, et al. Cholinergic Basal Forebrain Integrity and Cognition in Parkinson's Disease: A Reappraisal of Magnetic Resonance Imaging Evidence. Mov Disord. 2024 Dec;39(12):2155-2172. doi: 10.1002/mds.30023.

Schumacher J, Taylor JP, Hamilton CA, et al. In vivo nucleus basalis of Meynert degeneration in mild cognitive impairment with Lewy bodies. Neuroimage Clin. 2021;30:102604. doi: 10.1016/j.nicl.2021.102604.

Woo KA, Kim H, Kim R, et al. Cholinergic degeneration and early cognitive signs in prodromal Lewy body dementia. Alzheimers Dement. 2025 Feb;21(2):e14584. doi: 10.1002/alz.14584.

Novakova L, Gajdos M, Barton M, et al. Striato-cortical functional connectivity changes in mild cognitive impairment with Lewy bodies. Parkinsonism Relat Disord. 2024 Apr;121:106031. doi: 10.1016/j.parkreldis.2024.106031.

Kantarci K, Nedelska Z, Chen Q, et al. Longitudinal atrophy in prodromal dementia with Lewy bodies points to cholinergic degeneration. Brain Commun. 2022 Feb 7;4(2):fcac013. doi: 10.1093/braincomms/fcac013.

Železníková Ž, Nováková L, Vojtíšek L, et al. Early Changes in the Locus Coeruleus in Mild Cognitive Impairment with Lewy Bodies. Mov Disord. 2025 Feb;40(2):276-284. doi: 10.1002/mds.30058.

Ehrminger M, Latimier A, Pyatigorskaya N, et al. The coeruleus/subcoeruleus complex in idiopathic rapid eye movement sleep behaviour disorder. Brain. 2016 Apr;139(Pt 4):1180-8. doi: 10.1093/brain/aww006.

Theis H, Pavese N, Rektorová I, van Eimeren T. Imaging Biomarkers in Prodromal and Earliest Phases of Parkinson's Disease. J Parkinsons Dis. 2024;14(s2):S353-S365. doi: 10.3233/JPD-230385.

De Marzi R, Poewe W, Gizewski ER, Mahlknecht P, Seppi K. Utility of Nigral Signal Intensity Changes on MR Images to Differentiate Drug-induced Parkinsonism from Parkinson Disease. Radiology. 2016 Nov;281(2):651-652. doi: 10.1148/radiol.2016161491.

Tseriotis VS, Mavridis T, Eleftheriadou K, et al. Loss of the "swallow tail sign" on susceptibility-weighted imaging in the diagnosis of dementia with Lewy bodies: a systematic review and meta-analysis. J Neurol. 2024 Jul;271(7):3754-3763. doi: 10.1007/s00415-024-12381-6.

Tseriotis VS, Eleftheriadou K, Mavridis T, et al. Is the Swallow Tail Sign a Useful Imaging Biomarker in Clinical Neurology? A Systematic Review. Mov Disord Clin Pract. 2025 Feb;12(2):134-147. doi: 10.1002/mdc3.14304.

Chen Q, Boeve BF, Forghanian-Arani A, et al. MRI quantitative susceptibility mapping of the substantia nigra as an early biomarker for Lewy body disease. J Neuroimaging. 2021 Sep;31(5):1020-1027. doi: 10.1111/jon.12878. Epub 2021 May 25. PMID: 34033185; PMCID: PMC8440493.

Wang EW, Brown GL, Lewis MM, et al. Susceptibility Magnetic Resonance Imaging Correlates with Glial Density and Tau in the Substantia Nigra Pars Compacta. Mov Disord. 2023 Mar;38(3):464-473. doi: 10.1002/mds.29311.

Ofori E, Krismer F, Burciu RG, et al. Free water improves detection of changes in the substantia nigra in parkinsonism: A multisite study. Mov Disord. 2017 Oct;32(10):1457-1464. doi: 10.1002/mds.27100.

Burciu RG, Ofori E, Archer DB, et al. Progression marker of Parkinson's disease: a 4-year multi-site imaging study. Brain. 2017 Aug 1;140(8):2183-2192. doi: 10.1093/brain/awx146.

Chiu SY, Chen R, Wang WE, et al. Alzheimer's Disease Neuroimaging Initiative. Longitudinal Free-Water Changes in Dementia with Lewy Bodies. Mov Disord. 2024 May;39(5):836-846. doi: 10.1002/mds.29763.

Schumacher J, Ray NJ, Hamilton CA, et al. Free water imaging of the cholinergic system in dementia with Lewy bodies and Alzheimer's disease. Alzheimers Dement. 2023 Oct;19(10):4549-4563. doi: 10.1002/alz.13034.

Ye R, Goodheart AE, Locascio JJ, et al. Differential Vulnerability of Hippocampal Subfields to Amyloid and Tau Deposition in the Lewy Body Diseases. Neurology. 2024 Jun 25;102(12):e209460. doi: 10.1212/WNL.0000000000209460.

Sakurai K, Kaneda D, Morimoto S, et al. Medial temporal atrophy predicts the limbic comorbidities in lewy body disease. Neuroradiology. 2025 Jan;67(1):65-77. doi: 10.1007/s00234-024-03502-z.

Rennie A, Ekman U, Shams S, et al. Cerebrovascular and Alzheimer's disease biomarkers in dementia with Lewy bodies and other dementias. Brain Commun. 2024 Aug 28;6(5):fcae290. doi: 10.1093/braincomms/fcae290.

Cholinergic white matter and vascular pathology in Dementia with Lewy bodies: New insights from neuroimaging

Cene Jerele

Background

Dementia with Lewy bodies (DLB) is the second most common neurodegenerative dementia, frequently presenting with cerebrovascular disease (CVD) co-pathology that contributes to both neurodegeneration and clinical symptoms.[1] White matter signal abnormalities (WMSA) on magnetic resonance imaging (MRI) represent key markers of CVD, with their extent and localization potentially affecting cognitive function.[2] Particularly important are WMSA affecting cholinergic white matter pathways, which play a crucial role in cognition across various neurodegenerative conditions, including DLB.[3,4] Cholinergic pathways are affected early in DLB,[5] yet the relationship between WMSA and the cholinergic system in DLB remains poorly understood.

Neuroimaging Approaches to Assess Cholinergic Integrity

The Cholinergic Pathway Hyperintensities Scale (CHIPS) offers a feasible clinical tool for assessing WMSA in cholinergic pathways on MRI.[6] This semiquantitative visual rating scale evaluates WMSA in both medial (cingulum) and lateral (external capsule) cholinergic pathways, previously applied in Alzheimer's disease and Parkinson's disease but less studied in DLB. Our recent research compared CHIPS with other regional and global WMSA evaluation methods such as probabilistic tractography, FreeSurfer automated segmentation and Fazekas clinical scale to investigate the relationship between cholinergic white matter integrity, vascular pathology, and clinical manifestations in DLB.[7]

Key Findings from Recent Research

Cholinergic Pathway Involvement

Patients across the Lewy body (LB) continuum exhibited significantly higher WMSA burdens in cholinergic white matter compared to controls, particularly affecting the external capsule, while the cingulum showed more subtle involvement. These findings suggest a preferential vulnerability of certain cholinergic pathways to CVD co-pathology in DLB. The external capsule involvement was detected by both CHIPS and tractography-based mean diffusivity measures, while cingulum changes were only detected by the more sensitive tractography method.

Disease-Specific vs. Age-Related Changes

While global WMSA (assessed by Fazekas scale and FreeSurfer) reflected primarily age-related changes, cholinergic white matter abnormalities represented disease-specific findings in DLB. This distinction is clinically significant, suggesting that cholinergic pathways may be particularly vulnerable to WMSA in DLB, independent of overall white matter burden.

Association with Regional Brain Atrophy

CHIPS scores were associated with frontal atrophy in LB patients but not with medial temporal or posterior atrophy, suggesting that CVD-related cholinergic damage may specifically contribute to frontal neurodegeneration in DLB. In contrast, medial temporal atrophy appeared to be influenced by a combination of global CVD burden and possible Alzheimer's disease co-pathology.

Diagnostic Performance

CHIPS assessment of the posterior external capsule demonstrated high diagnostic performance (>80% sensitivity and specificity) for discriminating DLB patients from controls, comparable to research-grade tractography measures. This suggests potential clinical utility for CHIPS as an accessible biomarker.

Clinical Implications

These findings highlight the significant role of CVD co-pathology in cholinergic degeneration along the LB continuum. The association between cholinergic WMSA and frontal atrophy suggests that vascular changes may contribute to the clinical presentation of DLB beyond what would be expected from pure synucleinopathy.The differential involvement of cholinergic pathways—with earlier and more severe disruption of external capsule fibers compared to cingulum—aligns with recent evidence suggesting that cholinergic degeneration in Lewy body disease follows a posterior-to-anterior pattern.[8] This structured progression may have implications for the clinical staging and management of DLB. CHIPS presents an accessible clinical tool for assessing cholinergic white matter integrity, potentially aiding in the radiological characterization of DLB patients. Its strong correlation with more complex research methods like tractography supports its validity for clinical application.

Conclusion

Cerebrovascular co-pathology appears to be an important contributor to cholinergic degeneration in DLB, with a particular impact on the external capsule cholinergic pathway and frontal neurodegeneration. The CHIPS visual rating scale provides a clinically feasible method for assessing cholinergic white matter integrity in DLB, potentially enhancing diagnostic accuracy and treatment planning. These findings emphasize the importance of addressing vascular health in DLB management and suggest that targeted interventions for cerebrovascular risk factors might help preserve cholinergic function across the LB continuum.

REFERENCES

1. Watson R, Colloby SJ. Imaging in Dementia with Lewy Bodies: An Overview. J Geriatr Psychiatry Neurol. 2016;29(5):254-260. doi:10.1177/0891988716654984

2. De Reuck J, Maurage CA, Deramecourt V, et al. Aging and cerebrovascular lesions in pure and in mixed neurodegenerative and vascular dementia brains: A neuropathological study. Folia Neuropathol. 2018;56(2):81-87. doi:10.5114/fn.2018.76610

3. Burton EJ, McKeith IG, Burn DJ, Firbank MJ, O'Brien JT. Progression of white matter hyperintensities in Alzheimer disease, dementia with lewy bodies, and Parkinson disease dementia: a comparison with normal aging. Am J Geriatr Psychiatry. 2006;14(10):842-849. doi:10.1097/01.JGP.0000236596.56982.1C

4. Schumacher J, Ray NJ, Hamilton CA, et al. Free water imaging of the cholinergic system in dementia with Lewy bodies and Alzheimer's disease. Alzheimer's & Dementia. Published online March 15, 2023. doi:10.1002/alz.13034

5. Bohnen NI, Grothe MJ, Ray NJ, Müller MLTM, Teipel SJ. Recent Advances in Cholinergic Imaging and Cognitive Decline—Revisiting the Cholinergic Hypothesis of Dementia. Curr Geriatr Rep. 2018;7(1). doi:10.1007/s13670-018-0234-4

6. Bocti C, Swartz RH, Gao FQ, Sahlas DJ, Behl P, Black SE. A new visual rating scale to assess strategic white matter hyperintensities within cholinergic pathways in dementia. Stroke. 2005;36(10):2126-2131. doi:10.1161/01.STR.0000183615.07936.b6

7. Jerele C, Tzortzakakis A, et al. Cerebrovascular co-pathology and cholinergic white matter pathways along the Lewy body continuum. Manuscript accepted for publication in Brain Communications, 2025.

8. Okkels N, Grothe MJ, Taylor JP, et al. Cholinergic changes in Lewy body disease: implications for presentation, progression and subtypes. Brain. 2024;147(7):2308-2324. doi:10.1093/BRAIN/AWAE069

The role of neurophysiology in diagnosis and treatment of Dementia with Lewy bodies

Laura Bonanni, Anita D'Anselmo, Abhimanyu Mahajan, Alberto Jaramillo Jimenez

Electroencephalogram (EEG) is considered as an accurate biomarker for detecting neural changes related to dementia. The diagnostic potential of EEG is mainly due to its non-invasiveness, low cost, and high temporal resolution, which provides functional information in terms of cortical rhythm activity at millisecond levels. However, its spatial resolution is lower in comparison to other diagnostic techniques and, in clinical practice, qualitative EEG findings are subjected to visual interpretation by clinicians[1].

In neurodegenerative diseases, EEG exhibits a relevant role in detecting cognitive decline, also at early stages, and in discriminating different types of dementia[2–5]. In general, a common EEG finding in dementia is an increased slow activity together with a decreased rhythm in alpha frequency[6].

Among all dementing disorders, dementia with Lewy bodies (DLB) represents the second most common cause of dementia after Alzheimer's disease (AD)[7]. Nevertheless, slowing activities revealed by qualitative EEG are non-specific to DLB and may be observed in other neurodegenerative diseases or clinical conditions (e.g., alteration of state of consciousness, drug administrations)[8]. As a result, the introduction of quantitative EEG (QEEG), based on a computational approach to analyze EEG signals, has remarkably enhanced the diagnostic accuracy of this methodology[9]. Indeed, prominent posterior slow-wave activity on resting state EEG with periodic fluctuations in the pre-alpha/theta range has recently been included as a supportive biomarker for DLB diagnosis[10].

On EEG recordings, theta activity has previously been associated with the presence of cognitive decline, cognitive fluctuation (CF), and visual hallucinations (VHs)[11]. CF are clinically defined as spontaneous episodes of alterations in cognition, alertness, and attention, characterized also by hypersomnolence and impaired awareness of surroundings[12,13]. Notably, CF may occur in all forms of dementia, but its prevalence tends to increase up to 90% in case of DLB[14,15]. According to the most recent diagnostic criteria, CF is considered as a core clinical feature for DLB, together with VHs, parkinsonism, and REM sleep behavior disorder (RBD)[10]. However, CF has recently been designed to be more common and specifically related to DLB than clinical features as parkinsonism or VHs[16]. Therefore, the prominence of CF in DLB patients, as well as in Parkinson's disease with dementia (PDD), has strictly been correlated to Lewy body pathology and more recently to thalamic dysfunction, namely thalamocortical dysrhythmia (TCD)[11,14].

Nowadays, the diagnosis of DLB remains suboptimal and commonly misdiagnosed as AD. A critical point is to distinguish these two diseases at the earliest stages of dementia, since DLB patients are more sensitive to neuroleptic drugs, experience different responses to acetylcholinesterase inhibitors, and present a faster disease progression[17–19]. Therefore, considering the common difficulties in detecting DLB clinical symptoms such as CF, EEG reveals to be a promising and an effective diagnostic tool for reaching this goal, also at early stages of disease.

This talk will describe both spectral analysis approach and QEEG findings in DLB patients as a helpful guideline for clinicians to improve the application of this methodology in clinical setting. The concepts of TCD and QEEG analysis will be briefly introduced and, then, the results of QEEG in DLB, also at its prodromal stage, will be discussed.

A promising non-pharmacological intervention is transcranial electrical stimulation that has become so widespread in recent years, a non-invasive neurophysiological technique capable of modulating cortical excitability. Among the electrical stimulation techniques in particular, alternating current stimulation offers the possibility of modifying brain oscillations at specific frequencies through the application of a sinusoidal current that is able to induce a consequent effect on cognitive functions. Several studies have shown that the alpha rhythm is associated with various attentional mechanisms and in fact it has been seen that the application of alpha tACS can improve attentional performance20, 21.
Given these theoretical premises, the application of tACS to induce a modulation of resting oscillatory activity and modify cognitive performance in DLB patients will be discussed.

REFERENCES

1. Davidson PR, Jones RD, Peiris MTR, et al. EEG-based lapse detection with high temporal resolution. Suppl Clin Neurophysiol. 2013;54(5):832-839. doi:10.1109/TBME.2007.893452

2. Rosén I. Electroencephalography as a diagnostic tool in dementia. Dement Geriatr Cogn Disord. 1997;8(2):110-116. doi:10.1159/000106615

3. Henderson G, Ifeachor E, Hudson N, et al. Development and assessment of methods for detecting dementia using the human electroencephalogram. IEEE Trans Biomed Eng. 2006;53(8):1557-1568. doi:10.1109/TBME.2006.878067

4. Helkala EL, Laulumaa V, Soininen H, Partanen J, Riekkinen PJ. Different patterns of cognitive decline related to normal or deteriorating EEG in a 3-year follow-up study of patients with Alzheimer's disease. Neurology. 1991;41(4):528-532. doi:10.1212/wnl.41.4.528

5. Nardone R, Sebastianelli L, Versace V, et al. Usefulness of EEG Techniques in Distinguishing Frontotemporal Dementia from Alzheimer's Disease and Other Dementias. Dis Markers. 2018;2018. doi:10.1155/2018/6581490

6. Brunovsky M, Matousek M, Edman A, Cervena K, Krajca V. Objective assessment of the degree of dementia by means of EEG. Neuropsychobiology. 2003;48(1):19-26. doi:10.1159/000071824

7. McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology. 1996;47(5):1113-1124. doi:10.1212/wnl.47.5.1113

8. Britton JW, Frey LC, Hopp JL, et al. The Abnormal EEG. In Electroencephalography (EEG): An Introductory Text and Atlas of Normal and Abnormal Findings in Adults, Children, and Infants. (St. Louis EK, Frey LC, eds.).; 2016.

9. Bonanni L, Thomas A, Tiraboschi P, Perfetti B, Varanese S, Onofrj M. EEG comparisons in early Alzheimer's disease, dementia with Lewy bodies and Parkinson's disease with dementia patients with a 2-year follow-up. Brain. 2008;131(Pt 3):690-705. doi:10.1093/brain/awm322

10. McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. 2017;89(1):88-100. doi:10.1212/WNL.0000000000004058

11. Onofrj M, Espay AJ, Bonanni L, Delli Pizzi S, Sensi SL. Hallucinations, somatic-functional disorders of PD-DLB as expressions of thalamic dysfunction. Mov Disord. 2019;34(8):1100-1111. doi:10.1002/mds.27781

12. Ferman TJ, Smith GE, Boeve BF, et al. Specific features that reliably differentiate DLB from AD and normal aging. Neurology. 2004;62(2):181-187. doi:10.1212/WNL.62.2.181

13. Lee DR, Taylor J-P, Thomas AJ. Assessment of cognitive fluctuation in dementia: a systematic review of the literature. Int J Geriatr Psychiatry. 2012;27(10):989-998. doi:10.1002/gps.2823

14. McKeith IG, Dickson DW, Lowe J, et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. Neurology. 2005;65(12):1863-1872. doi:10.1212/01.wnl.0000187889.17253.b1

15. Byrne EJ, Lennox G, Lowe J, Godwin-Austen RB. Diffuse Lewy body disease: clinical features in 15 cases. J Neurol Neurosurg Psychiatry. 1989;52(6):709-717. doi:10.1136/jnnp.52.6.709

16. Bradshaw J, Saling M, Hopwood M, Anderson V, Brodtmann A. Fluctuating cognition in dementia with Lewy bodies and Alzheimer's disease is qualitatively distinct. J Neurol Neurosurg Psychiatry. 2004;75(3):382-387. doi:10.1136/jnnp.2002.002576

17. Ballard C, Grace J, McKeith I, Holmes C. Neuroleptic sensitivity in dementia with Lewy bodies and Alzheimer's disease. Lancet (London, England). 1998;351(9108):1032-1033. doi:10.1016/s0140-6736(05)78999-6

18. Olichney JM, Galasko D, Salmon DP, et al. Cognitive decline is faster in Lewy body variant than in Alzheimer's disease. Neurology. 1998;51(2):351-357. doi:10.1212/wnl.51.2.351

19. Levy R, Eagger S, Griffiths M, et al. Lewy bodies and response to tacrine in Alzheimer's disease. Lancet (London, England). 1994;343(8890):176. doi:10.1016/s0140-6736(94)90966-0

20. Helfrich RF, Knepper H, Nolte G, Strüber D, Rach S, Herrmann CS, et al. Selective modulation of interhemispheric functional connectivity by HD-tACS shapes perception. PLoS Biol. 2014;12(12):e1002031. doi: 10.1371/journal.pbio.1002031.

21. Tavakoli AV, Yun K. Transcranial Alternating Current Stimulation (tACS) Mechanisms and Protocols. Front Cell Neurosci. 2017 Sep 1;11:214. doi: 10.3389/fncel.2017.00214.

The role of molecular imaging in Dementia with Lewy bodies

Matej Perovnik, Maja Trošt

Introduction

Dementia with Lewy bodies (DLB) is a neurodegenerative disorder characterized by a combination of cognitive decline and parkinsonian features, with core clinical signs including fluctuations in cognition and visual hallucinations. In the diagnostic workup of DLB, multiple neuroimaging modalities are employed for both exclusion of other pathologies and identification of characteristic imaging features. Conventional structural imaging (CT or MRI) can reveal patterns of atrophy (notably a relative preservation of medial temporal lobe structures) that may support the diagnosis of DLB over dementia due to Alzheimer's disease (ADD). Functional imaging plays an important role in the next step of the diagnostic work-up. Positron emission tomography (PET), especially with 18F-fluorodeoxyglucose (FDG), can demonstrate metabolic deficits characteristic of DLB, and imaging of dopaminergic system, either with PET or single-photon emission computed tomography (SPECT), are frequently used to differentiate DLB from other dementias [1,2].

Metabolic brain imaging

Neuroimaging reveals both overlaps and important differences between DLB and other dementias like ADD and Parkinson's disease dementia (PDD). FDG PET scans in DLB characteristically show hypometabolism in the occipital lobes and in parieto-temporal regions, with relative sparing of the posterior cingulate cortex – a phenomenon known as the "cingulate island sign" [3]. This topography helps differentiate DLB from ADD, which usually presents with temporoparietal hypometabolism that includes the posterior cingulate without the involvement of the occipital cortex [3].

Clinically, the presence of occipital hypoperfusion or hypometabolism on SPECT/PET is now recognized as a supportive biomarker for DLB in consensus criteria [1]. Notably, the imaging profiles of DLB and PDD are largely overlapping given that they share the "core" pathology, namely α-synuclein deposits. Both DLB and PDD usually demonstrate reductions in occipital lobe activity on functional imaging and relatively mild medial temporal atrophy compared to ADD. Several studies showed greater cortical atrophy in DLB compared to PDD, even though the extent of these changes is heterogenous between studies and some studies found no differences [4]. Note that the current diagnostic criteria suggest following a so-called "one-year-rule" for differentiating between DLB and PDD, i.e. if the onset of dementia and parkinsonism occurs within one year, the patients should be diagnosed with DLB. There is some evidence that FDG PET might be of clinical use also for differentiation between DLB and PDD, while examining "only" regional changes. A longitudinal FDG PET-based study showed a marked decline in brain metabolism in posterior cortical regions in patients with DLB and in one of its prodromal forms, i.e. mild cognitive impairment due to LB (MCI-LB) compared to healthy individuals [5]. While a previous study suggested a more predominant subcortical, including the thalami, basal ganglia and hippocampus, changes in patients with PDD [6]. However, if cortical vs subcortical predominance could separate DLB from PDD cases remains to be investigated in the future.

For the practicing neurologist, these imaging observations have practical implications: preserved hippocampi on MRI or FDG PET or a prominent occipital hypometabolism on PET in a demented patient should raise suspicion for DLB over typical AD, while an abnormal dopamine transporter scan would support DLB/PDD over AD.

Metabolic brain network imaging

Beyond region-by-region findings, advanced multivariate imaging analyses have recently provided a more integrated picture of brain changes in DLB. Scaled Subprofile Modeling with Principal Component Analysis (SSM/PCA) is a network analysis technique that identifies covarying patterns of brain activity across subjects. Applied to FDG-PET scans, SSM/PCA can extract disease-specific metabolic networks whose expression can be then calculated at individual patient level (7). Using this approach, a so called DLB-related metabolic pattern (DLBRP) was identified. The DLBRP is characterized by a prominent hypometabolism in posterior cortical areas (notably the occipital cortex and inferior parietal lobes) coupled with relative hypermetabolism (persevered metabolic activity) in subcortical and limbic regions, such as the basal ganglia (putamen, pallidum), medial temporal structures (including the

hippocampi and parahippocampi), and the cerebellum. Importantly, the DLBRP shares partial topography with known AD and PD metabolic patterns, yet it bears distinct topographic characteristics [8]. This is consistent with DLB having elements of both AD (amyloid/tau co-pathology contributing to cortical hypometabolism) and PD (α-synuclein pathology driving subcortical network changes). Expression of the DLBRP can discriminate DLB patients from healthy controls with high accuracy, and also separates DLB from ADD [8]. The clinical relevance of identifying this network extends beyond diagnosis: the degree to which an individual expresses the DLB pattern correlates with disease severity and has been linked to shorter survival time [8]. Interestingly, a metabolic brain pattern related to cognitive dysfunction in PD, so called PD-cognitive pattern (PDCP) is topographically unrelated to DLBRP and is characterized by a more prominent frontal hypometabolic changes [9]. Network imaging analysis offers an additional information and provide a tool for precise quantification of disease-specific changes at an individual level. This is also reflected in the most recent joint statement of the Society of Nuclear Medicine and Molecular Imaging and the EANM, which lists multivariate image analysis, based on SSM/PCA, as a possible aid for FDG PET image analysis [10].

Amyloid PET

A shared feature of neurodegenerative diseases causing dementia including DLB is the abnormal accumulation and spreading of pathological protein aggregates. They affect the selective vulnerable functional circuits in a disease-specific pattern [11]. DLB has extensive clinical, pathological and genetic overlap with PDD and it commonly co-exists with AD neuropathology, which is characterized by the abnormal accumulation of amyloid beta (Aβ) plaques and neurofibrillary tangles of hyperphosphorylated tau (tau) [12]. Between 51 and 73% of patients with Lewy body dementias (LBD), i.e. either DLB or PDD, meet consensus criteria for AD at autopsy [13,14]. Amyloid plaques can be visualized in patient's brain by amyloid PET in vivo.

Amyloid PET has been established as an important imaging tool in early and specific diagnosis of AD. It is also part of the biomarker screening in the AD diagnostic criteria and can help differentiate from other dementias [15]. There are several amyloid PET tracers currently available for use, namely 11C-Pittsburgh compound–B (PiB), 18F-flutemetamol, 18F-florbetaben, 18F-florbetapir that bind to Aβ plaques and have been validated through autopsy studies. However, we must be aware that amyloid PET cannot be easily used for the differential diagnosis of AD and DLB, that are two of the most common types of dementia [16].

However, recent advances in understanding of pathology [17] have revealed that lower PiB uptake accurately distinguishes cases with Lewy body disease (LBD) from cases with AD or mixed pathology. The severity of diffuse amyloid pathology is therefore the primary contributor to elevated PiB uptake in LBD.

It has been discovered that AD co-pathology in LBD (DLB+) is associated with poorer cognition, greater medial temporal lobe atrophy and a reduced prevalence of visual hallucinations and parkinsonism in cross-sectional studies. However, the relationship between Aβ and tau biomarkers and longitudinal disease trajectory in LBD is less clear, with some studies reporting poorer outcome and some not [12]. Pathology studies have shown increased mortality in LBD+ compared to LBD- as well as seven years shorter overall survival [12]. There was also an association between increased amyloid and tau burden in LBD and accelerated MMSE decline. Interestingly, this is not so clear for PD [12].

Imaging studies too, confirm strong evidence that greater amyloid PET positivity is associated with accelerated cognitive and functional decline in DLB. A robust study demonstrated an association between greater tau accumulation in specific brain regions and cognitive decline in DLB [18]. Given that amyloid β radiotracer binding correlates well with neuritic plaque and neurofibrillary tangle burden in LBD, the PET literature suggests accelerated disease progression in LBD+.

CSF studies report discrepant findings and limited number of plasma biomarker studies in LBD currently preclude from making a definitive conclusion.

Although there are some discrepancies in the literature no studies reported an association of AD co-pathology and better outcomes. The most reported outcome was cognitive decline. The estimated mean difference between LBD+ and LBD- ranged from 0.53 to 2.9 additional MMSE points/year [12]. LBD+ demonstrated increased cognitive decline, functional decline, mortality and poorer response to treatment compared to LBD-. These results suggest that AD co-pathology in LBD accelerates disease progression in a clinically significant manner.

Regarding α-synuclein (α-syn) neuropathology studies have established that greater α-syn burden is correlated with conversion to dementia [19,20] and disease duration independently of AD co-pathology in LBD. Similarly, a big majority of studies that quantified α-syn, found this to be significantly correlated to poorer clinical outcomes. This raises the question of the role of AD co-pathology. It may accelerate α-syn aggregation, but AD co-pathology may also be an independent driver of neuronal dysfunction and death.

Dopamine transporter imaging

DLB often features nigrostriatal dopaminergic degeneration that can be detected in vivo using 123I-FP-CIT dopamine transporter single photon emission computed tomography (DaT SPECT). Clinically, this dopamine transporter imaging has become an important supportive biomarker to distinguish DLB from other dementias. In DLB, the DaT SPECT typically shows significantly reduced striatal uptake of the tracer, reflecting loss of dopamine transporters, whereas in AD, a normal striatal DAT binding is observed. Thus, an abnormal DaT SPECT strongly favors a LBD over AD, and studies over the past decade consistently demonstrate high diagnostic accuracy for DLB (sensitivity ~85–88%, specificity ~90–100%) when differentiating it from AD [(4)]. By contrast, PDD shows a similar marked reduction in striatal DAT binding as DLB [(4)].
In summary, molecular imaging techniques, such as FDG PET, amyloid PET, and DaT SPECT, have an important role in early as well as differential diagnostic workup in patients with suspected DLB. Further, molecular imaging techniques add an important information about the underlying pathophysiology and prognosis of DLB patients on an individual basis.

REFERENCES

1. McKeith IG, Boeve BF, Dickson DW, Halliday G, Taylor J-P, Weintraub D, et al. Diagnosis and management of dementia with Lewy bodies Fourth consensus report of the DLB Consortium. Neurology [Internet]. 2017 Jul 4;89(1):88–100. Available from: http://www.neurology.org/lookup/-doi/10.1212/WNL.0000000000004058

2. Watson R, Colloby SJ. Imaging in Dementia with Lewy Bodies: An Overview. J Geriatr Psychiatry Neurol. 2016;29(5):254–60.

3. Brown RKJ, Bohnen NI, Wong KK, Minoshima S, Frey KA. Brain PET in Suspected Dementia: Patterns of Altered FDG Metabolism. RadioGraphics [Internet]. 2014 May;34(3):684–701. Available from: http://pubs.rsna.org/-doi/10.1148/rg.343135065

4. Yousaf T, Dervenoulas G, Valkimadi P-E, Politis M. Neuroimaging in Lewy body dementia. J Neurol [Internet]. 2019 Jan 14;266(1):1–26. Available from: http://dx.doi.org/10.1007/s00415-018-8892-x

5. Ferreira D, Przybelski SA, Lesnick TG, Diaz-Galvan P, Schwarz CG, Murray MM, et al. Longitudinal FDG-PET Metabolic Change Along the Lewy Body Continuum. JAMA Neurol [Internet]. 2025 Jan 13;55905:1–10. Available from: https://jamanetwork.com/journals/jamaneurology/fullarticle/2828605

6. Bohnen NI, Koeppe RA, Minoshima S, Giordani B, Albin RL, Frey KA, et al. Cerebral Glucose Metabolic Features of Parkinson Disease and Incident Dementia: Longitudinal Study. J Nucl Med [Internet]. 2011 Jun 1;52(6):848–55. Available from: http://jnm.snmjournals.org/cgi/doi/10.2967/jnumed.111.089946

7. Perovnik M, Rus T, Schindlbeck KA, Eidelberg D. Functional brain networks in the evaluation of patients with neurodegenerative disorders. Nat Rev Neurol [Internet]. 2023 Feb 20;19(2):73–90. Available from: https://www.nature.com/articles/s41582-022-00753-3

8. Perovnik M, Tomše P, Jamšek J, Tang C, Eidelberg D, Trošt M. Metabolic brain pattern in dementia with Lewy bodies: Relationship to Alzheimer's disease topography. NeuroImage Clin [Internet]. 2022;35:103080. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2213158222001450

9. Trošt M, Perovnik M, Pirtošek Z. Correlations of Neuropsychological and Metabolic Brain Changes in Parkinson's Disease and Other α-Synucleinopathies. Front Neurol [Internet]. 2019 Nov 14;10:1204. Available from: https://www.frontiersin.org/article/10.3389/fneur.2019.01204/full

10. Arbizu J, Morbelli S, Minoshima S, Barthel H, Kuo P, Van Weehaeghe D, et al. SNMMI Procedure Standard/EANM Practice Guideline for Brain [18 F]FDG PET Imaging, Version 2.0. J Nucl Med [Internet]. 2024 Oct 17;64(2):-jnumed.124.268754. Available from: http://jnm.snmjournals.org/lookup/-doi/10.2967/jnumed.124.268754

11. Ni R, Nitsch RM. Recent Developments in Positron Emission Tomography Tracers for Proteinopathies Imaging in Dementia. Front Aging Neurosci [Internet]. 2022 Jan 3;13. Available from: https://www.frontiersin.org/articles/10.3389/fnagi.2021.751897/full

12. Tan JH, Laurell AA, Sidhom E, Rowe JB, O'Brien JT. The effect of Amyloid and Tau Co-pathology on disease progression in Lewy body dementia: A systematic review. Parkinsonism Relat Disord [Internet]. 2025 Feb;131:107255. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1353802024012677

13. Graff-Radford J, Aakre J, Savica R, Boeve B, Kremers WK, Ferman TJ, et al. Duration and Pathologic Correlates of Lewy Body Disease. JAMA Neurol [Internet]. 2017 Mar 1;74(3):310. Available from: http://archneur.jamanetwork.com/article.aspx?doi=10.1001/jamaneurol.2016.4926

14. Irwin DJ, Grossman M, Weintraub D, Hurtig HI, Duda JE, Xie SX, et al. Neuropathological and genetic correlates of survival and dementia onset in synucleinopathies: a retrospective analysis. Lancet Neurol [Internet]. 2017 Jan;16(1):55–65. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1474442216302915

15. Chouliaras L, O'Brien JT. The use of neuroimaging techniques in the early and differential diagnosis of dementia. Mol Psychiatry [Internet]. 2023 Oct 22;28(10):4084–97. Available from: https://www.nature.com/articles/s41380-023-02215-8

16. Donaghy PC, Firbank MJ, Thomas AJ, Lloyd J, Petrides G, Barnett N, et al. Amyloid Imaging and Longitudinal Clinical Progression in Dementia With Lewy Bodies. Am J Geriatr Psychiatry [Internet]. 2020 May;28(5):573–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1064748119305895

17. Kantarci K, Lowe VJ, Chen Q, Przybelski SA, Lesnick TG, Schwarz CG, et al. β-Amyloid PET and neuropathology in dementia with Lewy bodies. Neurology [Internet]. 2020 Jan 21;94(3):e282–91. Available from: http://www.neurology.org/-lookup/doi/10.1212/WNL.0000000000008818

18. Chen Q, Przybelski SA, Senjem ML, Schwarz CG, Lesnick TG, Botha H, et al. Longitudinal Tau Positron Emission Tomography in Dementia with Lewy Bodies. Mov Disord [Internet]. 2022 Jun 8;37(6):1256–64. Available from: https://movementdisorders.onlinelibrary.wiley.com/doi/10.1002/mds.28973

19. Schneider JA, Arvanitakis Z, Yu L, Boyle PA, Leurgans SE, Bennett DA. Cognitive impairment, decline and fluctuations in older community-dwelling subjects with Lewy bodies. Brain [Internet]. 2012 Oct 1;135(10):3005–14. Available from: https://academic.oup.com/brain/article-lookup/-doi/10.1093/brain/aws234

20. Ruffmann C, Calboli FCF, Bravi I, Gveric D, Curry LK, de Smith A, et al. Cortical Lewy bodies and Aβ burden are associated with prevalence and timing of dementia in Lewy body diseases. Neuropathol Appl Neurobiol [Internet]. 2016 Aug 2;42(5):436–50. Available from: https://onlinelibrary.wiley.com/-doi/10.1111/nan.12294

NAPREDOVALA OBLIKA PARKINSONOVE BOLEZNI?

Morda gre pri takšnem bolniku za stopnjo Parkinsonove bolezni, pri kateri bi bilo koristno spremeniti način zdravljenja.

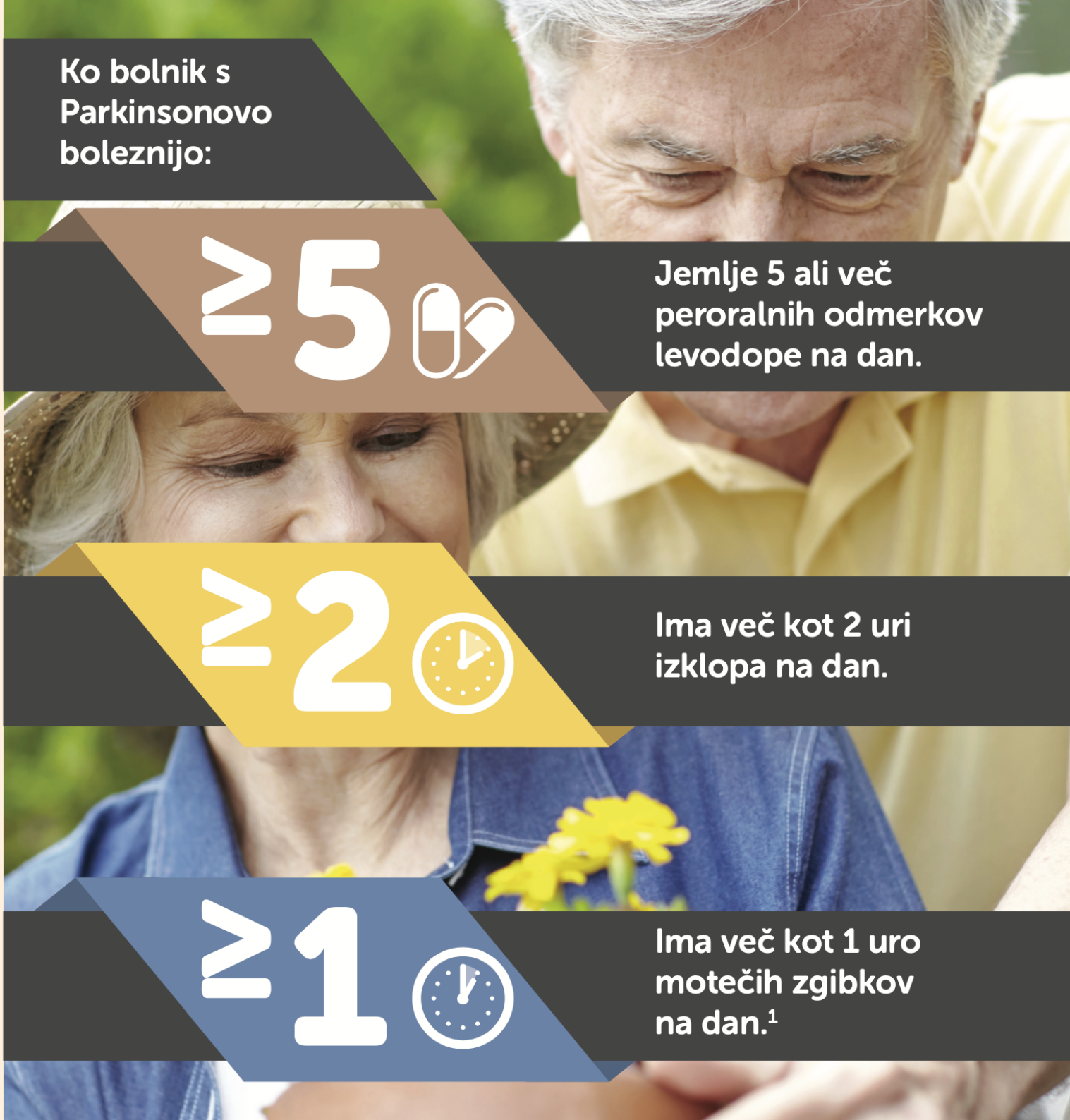
Priporočen je posvet z osebnim nevrologom in razmislek o možnostih napotitve v specializiran center za bolnike s Parkinsonovo boleznijo na Nevrološki kliniki Ljubljana ali na Oddelku za nevrološke bolezni UKC Maribor.

Material je pripravljen v sodelovanju z Nevrološko kliniko Ljubljana.
Datum priprave informacije: april 2025
Kontaktni podatki: Abbvie Biofarmacevtska družba d.o.o., Dolenjska cesta 242c, 1000 Ljubljana, Slovenija

Vir: Angelo Antonini et al., Developing consensus among movement disorder specialists on clinical indicators for identification and management of advanced Parkinson's disease: a multi-country Delphi-panel approach, CURRENT MEDICAL RESEARCH AND OPINION 2018, VOL. 34, NO. 12, 2063–2073.

SI-NEUP-250017

abbvie

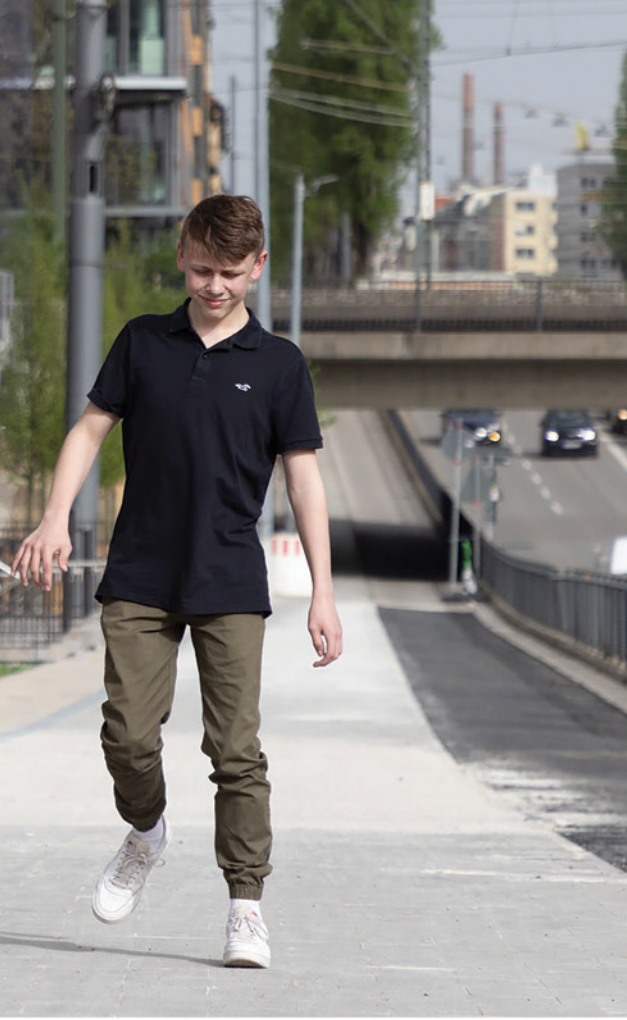


Ali bi prepoznali bolnika s FRIEDREICHOVO ATAKSIJO (FA)?

Friedreichova ataksija (FA) je progresivna nevrodegenerativna bolezen, ki velja za najpogostejšo avtosomno recesivno dedno ataksijo.[1,2]

Pomislite tudi na **Friedreichovo ataksijo,** če pri bolniku opazite enega ali kombinacijo simptomov:[1,2]

TEŽAVO S HOJO IN MOTNJO KOORDINACIJE | **MOTNJO RAVNOTEŽJA** | **IZGUBO SENZORIKE** | **NERAZLOČEN GOVOR**



Bolniki s FA imajo lahko tudi:[1,2]

• **DIABETES,** • **KARDIOMIOPATIJO,** • **PES CAVUS,** • **SKOLIOZO**

Za postavitev diagnoze je ključna izbira genetskega testa, namenjenega testiranju izključno na FA.[3,4]

Bolnika s sumom na FA napotite v ambulanto za živčno-mišične bolezni na **Klinični inštitut za klinično nevrofiziologijo Univerzitetnega kliničnega centra Ljubljana.**

Več o Friedreichovi ataksiji najdete na naši spletni strani:

Viri:1. Schulz JB, Boesch S, Bürk K, et al. Diagnosis and treatment of Friedreich ataxia: a European perspective. Nat Rev Neurol. 200 9;5(4):222–234. | **2.** Williams CT, De Jesus O. Friedreich Ataxia. 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. | **3.** Fogel BL, Perlman S. Clinical features and molecular genetics of autosomal recessive cerebellar ataxias. Lancet Neurol. 2007;6(3):245–257. | **4.** Bidichandani SI, Delatycki MB. Friedreich Ataxia. 1998 Dec 18 [Updated 2017 Jun 1]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; Last Update: October 31, 2024. Dostopno na: https://www.ncbi.nlm.nih.gov/ books/ NBK1281/. Dostopano: april 2025.

Podrobnejše informacije so na voljo pri: Biogen Pharma d. o. o., Ameriška ulica 8, 1000 Ljubljana, Slovenija, tel.: 01 511 02 90
www.biogen-pharma.si • Datum priprave informacije: april 2025 • Samo za strokovno javnost • Biogen-262162

Biogen

The 13th COGNITIVE DAY meeting was made possible by

Main sponsor
ABBVIE d.o.o.

Organisers
Center for Cognitive Impairments, Department of Neurology, University Medical Centre Ljubljana

Slovenian Neurological Association

Main sponsor
Biogen Pharma d.o.o.

Sponsors

ALKALOID - FARM d.o.o.

KRKA d.d.

MEDIS d.o.o.

STADA d.o.o.

TEVA / PLIVA LJUBLJANA d.o.o.