Clinical Onset Patterns and Symptom Associations in prodromal Dementia with Lewy Bodies: a single-center retrospective study

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BACKGROUND

Dementia with Lewy bodies (DLB) is the second most common neurodegenerative dementia after Alzheimer's disease (AD), but there is limited information regarding the prodromal DLB state compared with that of AD..

The prodromal stage of DLB [1]. Includes **different possible onset presentations (OPs)**:

- Mild Cognitive Impairment (MCI-LB),
- Psychiatric-onset
- Delirium-onset

Moreover, several **core** (cognitive fluctuations, CF; Visual Hallucinations, VH; REM Behavior Disorder, RBD; Parkinsonism) and supportive clinical features (such as hyposmia and dysautonomia) but their prevalence and associations have not been thoroughly studied.

AIMS and METHODS

In the present study we aimed to:

1) Retrospectively characterize the clinical OPs of DLB and explore the distribution and associations of core and supportive clinical features across different onset subtypes.
2) Explore the distribution and associations of core and supportive clinical features

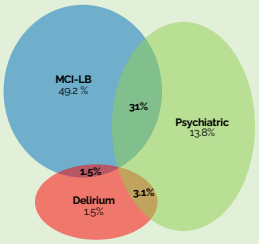
Sample Selection: We retrospecticely enrolled 65 patients with DLB from the «CLIMB-DLB» cohort

Data Collection: Clinical history was collected from the medical charts of patients focusing on the type of OPs and the absence/presence of core and supportive clinical features at the time of onset

Statistycal Analysis: The X2-test was used to assess differences in the prevalence of clinical features between OPs, Phi coefficient (φ) matrix was used to assess associations between clinical features and 2x2 contingency tables were used to calculate odds ratios of significant associations

RESULTS

1 DISTRIBUTION AND OVERLAPS BETWEEN OPs



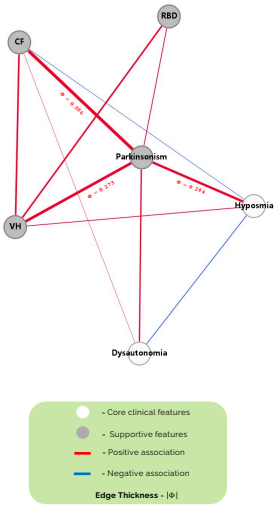
- MCI-LB was the most frequent OP [2]
- Overlaps of OPs were quite common, in particular the most frequent was the one between MCI and Psychiatric onset

2 PREVALENCE OF CLINICAL FEATURES BETWEEN OPs

	ALL	MCI-LB	PSY	DELIRIUM	p
RBD	46%	52.3%	28.6%	50%	0.299
VH	31%	34.1%	28.6%	25%	0.882
CF	8.1%	6.8%	14.2%	0%	0.556
Parkinsonism	31%	29.6%	42.9%	0%	0.250
Dysautonomia	11%	9.1%	7.1%	0%	0.807
Hyposmia	6%	9.1%	0%	0%	0.417

Abbreviations: RBD= Rem Behavior Disorder; VH= Visual Hallucinations; CF= Cognitive Fluctuations; PSY= Psychiatric-Onset

3 NETWORK DIAGRAM OF THE ASSOCIATIONS OF CLINICAL FEATURES



4 CONTINGENCY TABLES OF THE SIGNIFICANT ASSOCIATIONS BETWEEN CLINICAL FEATURES

		Parkinsonism		OR	p
		Yes	No		
Cognitive Fluctuations	Yes	20%	2.3%	10.4	0.014*
	No	80%	97.7%		
Visual Hallucinations	Yes	50%	22.3%	3.4	0.029*
	No	50%	77.3%		
Hyposmia	Yes	15%	2.3%	1.7	0.082
	No	85%	97.7%		

On the right:
The network diagram shows the associations between clinical features and their strenght. We found significant associations between parkinsonism and both CF and VH
Phi coefficient (φ) value of significant associations is shown

On the left:
Table for Odds Ratios derived from contingency tables of the significant associations between core and clinical features

DISCUSSION

- ✓ Association between MCI and psychiatric onset was relatively common, suggesting that **overlapping features at onset may further support the diagnosis of DLB**.
- ✓ Significant association between **parkinsonism and both CF and VH**, highlighting a tendency for these symptoms to co-occur. Moreover, a weaker trend for parkinsonism to occurr with hyposmia was also found. This supports the existence of shared mechanisms possibly underlied by different pathways of alpha-synuclein spreading.

Limitations

The analysis on the CLIMB-DLB cohort was **retrospective** and focused on the onset time, moreover we assessed the binary presence of the core and supportive clinical features without **quantifying** their severity

CONCLUSIONS

Overall, this study suggests that specific patterns of clinical features occur in prodromal DLB, a well-known multi-faceted clinical entity

These finding provides a basis for further investigation into the underlying mechanisms of this association, possibly linked to different alpha-synuclein spreading pathways.

1. I. G. McKeith et al., "Research criteria for the diagnosis of prodromal dementia with Lewy bodies," Neurology, vol. 94, no. 17, pp. 743–755, 2020, doi: 10.1212/WNL.0000000000009323
2. K. A. Wyman-Chick et al., "Prodromal Dementia With Lewy Bodies: Evolution of Symptoms and Predictors of Dementia Onset," *J Geriatr Psychiatry Neurol*, vol. 35, no. 4, pp. 527–534, 2022, doi: 10.1177/08919887211023586.

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