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Dementia with Lewy bodies subtypes identified by cluster analysis on structural MRI

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Abstract

Background: Dementia with Lewy bodies (DLB) is a neurodegenerative disorder that presents with a variety of clinical symptoms. Part of the clinical heterogeneity within DLB has been related to the atrophy/sparing of the hippocampus. We extended that previous research by investigating whether different atrophy patterns exist in DLB, beyond and above the atrophy/sparing of the hippocampus, and whether those patterns contribute to the clinical heterogeneity in DLB. We aimed to identify DLB atrophy subtypes using a hypothesis-free data-driven clustering approach based on regional gray matter (GM) volumes and characterize the resulting subtypes across key measures.

Method: We included data from three centers of the European DLB consortium. A high-resolution 3D T1-weigthed magnetization prepared rapid gradient echo (MPRAGE) sequence was acquired for 97 DLB patients. Eighty-four cortical regions and 12 subcortical regions from Mayo Clinic Adult Lifespan Template (https://www.nitrc.org/projects/mcalt/) atlases were obtained. Clusters of DLB patients were then determined using the random forest method. Between-group differences in key demographic, clinical, MRI volumes and cerebrospinal fluid biomarkers (CSF) (amyloid-beta, phosphorylated-tau) were performed for clusters characterization.

Result: We identified three subtypes of DLB patients, with distinct patterns of GM volumes and differences in several clinical and demographic measures. Cluster 1 (C1) included 32 DLB patients (33%), cluster 2 (C2) included 29 DLB patients (30%), and cluster 3 (C3) included 36 DLB patients (37%). The clusters differed in age, with C1 being significantly older (72±8.6) than C3 (66±9.5) (F=3.93, p=0.02). C1 was characterized by lower volumes in fronto-temporal regions and had a higher frequency of

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visual hallucinations (68%, vs. C2 35%). C2 showed lower volumes in occipital regions. C3 had higher GM volumes overall compared with the other two clusters and presented with a higher frequency of cognitive fluctuations (91%, vs. C1 67%). There were no differences between groups in CSF biomarkers. These results were independent of cluster differences in age and global GM volume.

Conclusion: There are distinct patterns of brain atrophy in patients with DLB. These patterns seem to differentially contribute to the frequencies of visual hallucinations and cognitive fluctuations, independently of differences in age and global GM volume across subtypes.

TABLE 1

	C1 (N=32)	C2 (N=29)	C3 (N=36)	ANOVA (p-value)	post-hoc
sex (male/female)	20/12	22/7	20/16	1.46 (0.24)	
Age	71.9 (8.6)	68.7 (7.8)	65.9 (9.5)	3.93 (0.02)	C1 vs C3
Years of education	12.4 (3.3)	12.5 (4.8)	12.2 (4)	0.06 (0.94)	
MMSE	22.8 (4.7)	22.9 (4.7)	24.8 (3.9)	2.41 (0.09)	
Visual hallucinatinos (yes/no)	21/10 (68%)	10/19 (35%)	16/20 (44%)	3.72 (0.03)	C1 vs C2
Cognitive fluctuations (yes/no)	20/10 (67%)	24/3 (89%)	31/3 (91%)	4.08 (0.02)	C1 vs C3
Parkinsonism (yes/no)	30/2 (94%)	22/7 (76%)	28/8 (78%)	2.15 (0.12)	
Rapid-eye movement behavior disorder (yes/no)	21/9 (70%)	20/5 (80%)	15/14 (52%)	2.60 (0.08)	
Amyloid-beta (yes/no)	9/21 (30%)	7/22 (24%)	11/25 (31%)	0.18 (0.83)	
Phosphorylated-tau (yes/no)	13/17 (43%)	10/19 (34%)	12/24 (33%)	0.39 (0.68)	