

The Clinical Presentation Of Amygdala Predominant Lewy Body Pathology

PC Donaghy¹, K Olsen¹, L Patterson¹, L Palmer², C Tasman², C Troakes³, S Downes³, S Al-Sarraj^{3,4}, AJ Thomas¹, JP Taylor¹, CA Hamilton¹, RA Lawson¹, A Yarnall¹, T Outeiro¹, CM Morris¹.

1. NIHR Newcastle Biomedical Research Centre, Newcastle University, UK
2. South West Dementia Brain Bank, University of Bristol, UK.
3. London Neurodegenerative Diseases Brain Bank, King’s College London, UK.
4. Department of Clinical Neuropathology, King’s College Hospital, London, UK.

Amygdala predominant Lewy body pathology is associated with intermediate findings on quantitative alpha-synuclein seeding assay, high rates of apathy and relatively rapid cognitive decline.

INTRODUCTION

Amygdala predominant Lewy body pathology (APLBP)¹ is a common postmortem finding in cases with Alzheimer’s disease (AD) pathology.^{2,3} It is currently unclear whether APLBP contributes to cognitive impairment and symptom presentation, and therefore whether targeting alpha-synuclein (aSyn) is likely to be an effective therapeutic strategy in people with APLBP. This has become increasingly important as aSyn seed-aggregation assays (SAAs) are positive in up to 50% of cases of APLBP.⁴⁻⁶

METHODS

Clinical records were examined from 227 pathologically defined cases:

- APLBP¹
- AD (Braak Neurofibrillary Tangle (NFT) ≥5 and Braak LB 0)
- LB/AD- (limbic/neocortical LB pathology and Braak NFT stage ≤III)
- LB/AD+ (limbic/neocortical LB pathology and Braak NFT ≥IV)
- Controls

An alpha synuclein seeding assay was carried out on extracellular vesicles derived from post mortem CSF⁷ in a wider sample of 254 participants.

RESULTS

	APLBP	AD	LB/AD-	LB/AD+	Control
n	56	45	41	43	42
Age at death (years)	80.3 (9.3)	83.2 (6.9)	80.5 (7.4)	80.7 (7.6)	83.2 (9.1)
Sex male	55%	58%	59%	61%	52%
Clinical diagnosis LB disease	4%	4%	54%	33%	0%
First MMSE score	21.5 (7.8)	21.1 (8.2)	24.8 (4.6)	23.2 (6.3)	28.7 (1.5)*
MMSE change/year	-2.9 (1.9)	-2.2 (1.8)	-1.0 (1.7)*	-2.2 (1.4)	-0.2 (0.6)*
aSyn SAA +ve	97 %	29 %	100 %	100 %	12 %
SAA lag phase (h)	72.4 (17.5)	116.1 (28.2)*	59.1 (9.0)*	60.6 (10.9)	127.6 (21.9)*
SAA slope	20.5 (17.5)	4.8 (5.4)*	26.4 (7.9)*	26.8 (9.3)*	3.4 (4.1)*
SAA Maximum RFU	2823 (2738)	661 (606)*	2943 (1017)	3052 (1041)	484 (563)*
SAA AUC (x10 ⁸)	4.02 (3.37)	1.04 (1.27)*	5.78 (2.19)*	5.92 (2.35)*	0.71 (0.76)*

Table 1. Demographics and α-synuclein seed amplification assay results.

Mean (SD) or percentage. APLBP amygdala predominant Lewy body pathology; AD Alzheimer’s disease; LB Lewy body; aSyn α-synuclein; AUC area under curve; MMSE Mini-Mental State Examination; RFU relative fluorescence units; SAA seed amplification assay. * p<.05 v APLBP

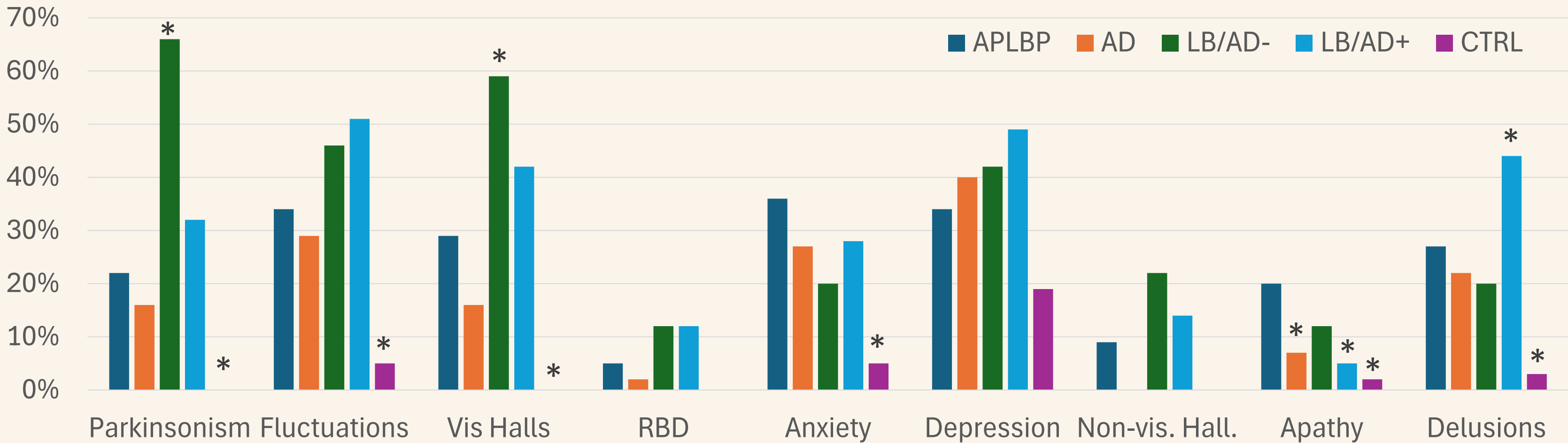


Figure 1. Core clinical features and psychiatric symptoms.

APLBP amygdala predominant Lewy body pathology; AD Alzheimer’s disease; LB Lewy body; Vis. Hall visual hallucinations; RBD REM sleep behaviour disorder. * =p<.05 v APLBP

CONCLUSIONS

APLBP is associated with distinct clinical features and biomarker profile. Quantitative findings from SAA show a profile intermediate between AD and LB. Similarly, rates of core clinical features of LB disease in APLBP are intermediate between AD and LB. However, apathy appears to be particularly common in APLBP. These findings have clear implications for clinical trials in AD and LB disease that may include people with APLBP. In AD trials, participants with comorbid APLBP may represent a group with a greater apathy and relatively rapid cognitive decline. In trials in cognitive impairment in LB disease, APLBP may represent a group with relatively low burden of core clinical features.

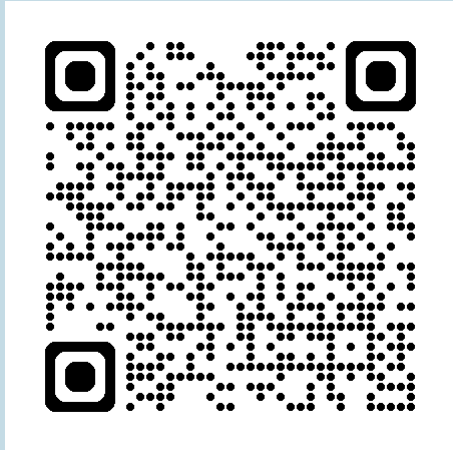
Further work is required in cohorts with in vivo CSF samples and striatal dopaminergic imaging to understand how APBLP aligns with current proposed criteria for biological classification of synucleinopathies.

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CONTACT

paul.donaghy@ncl.ac.uk



This work is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre: Newcastle (NIHR203309)
The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.