T1 MRI reveals differential hippocampal atrophy in Lewy Body Disorders with and without Alzheimer's copathology

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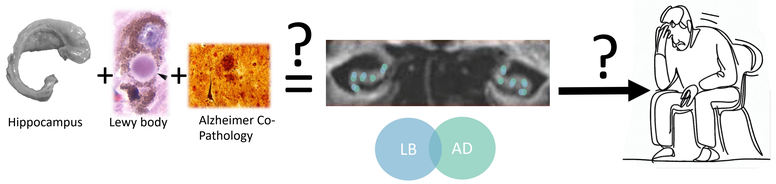
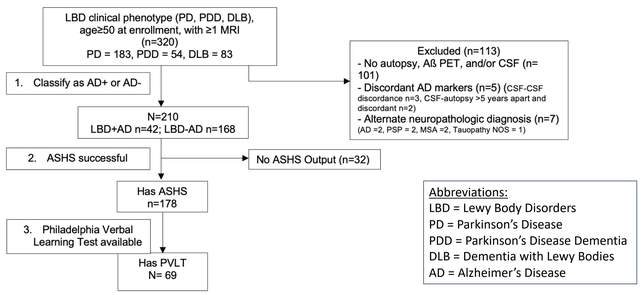
Background

- ~50% of LBD patients have AD co-pathology (LBD+AD) which is associated with shorter time to dementia and death.
- However, little is known about the selective distribution of hippocampal atrophy associated with LBD+AD and its contribution to verbal memory performance.

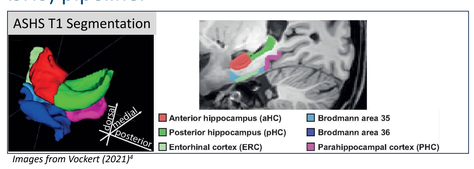


Methods

- 178 patients with clinical diagnoses of LBD (PD, n = 111; PDD, n = 27; DLB, n = 40) with available T1 MRI and AD biomarkers or autopsy, were identified from the Penn Integrated Neurodegenerative Disease Database.



- Cognitively-normal historical controls from Alzheimer's Disease Neuroimaging Initiative[3] were used for comparison (n=190).
- AD copathology was defined hierarchically by: a) AD "intermediate" or "high" by ABC neuropathologic criteria (n = 40); 2) positive amyloid PET (n=2); or 3) CSF total tau:β-amyloid1-42 ratio > 0.3 (autopsy-validated cutpoint) (n=136).
- T1 MRIs processed using the Automated Segmentation of Hippocampal Subfields (ASHS) pipeline.



Images from Vockert (2021)[4]

- Hippocampal volume (HV) and adjacent cortical thickness was compared between controls, LBD-AD, and LBD+AD, and correlated with verbal memory scores.
- Linear regression was used to test the association of AD copathology and HV (dependent variable), covarying for age, sex, and intracranial volume.

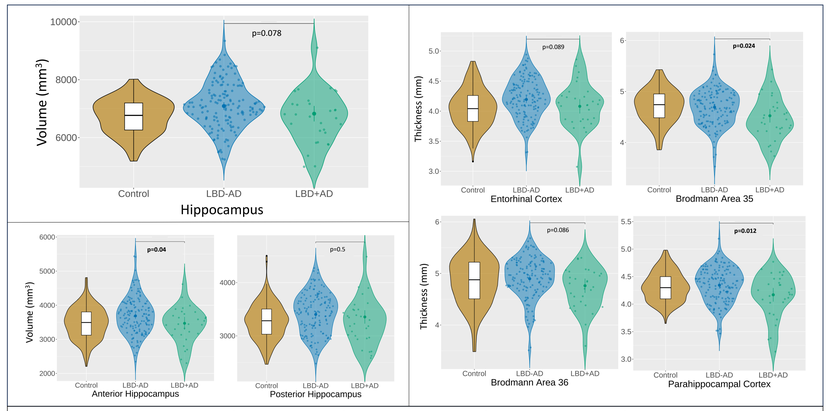
Results

Table 1: Demographics and Clinical Characteristics

	Control* (N=190)	LBD-AD (N=148)	LBD+AD (N=30)	All LBD (N=178)	*p*
Age at MRI: Mean (SD)	72.3 (6.0)	66.7 (7.58)	72.1 (5.74)	67.6 (7.56)	**<0.001**
Sex: Males (%)	100 (52.6)	108 (73.0%)	19 (63.3%)	127 (71.3%)	0.4
Race: White (%)	-	142 (95.9%)	29 (96.7%)	171 (96.1%)	1
Education: (Years) Mean (SD)	16.9 (2.4)	16.0 (2.36)	15.0 (2.86)	15.8 (2.48)	*0.066*
Diagnosis					
DLB	-	27 (18.2%)	13 (43.3%)	40 (22.5%)	
PDD	-	20 (13.5%)	7 (23.3%)	27 (15.2%)	**0.001**
PD	-	101 (68.2%)	10 (33.3%)	111 (62.4%)	
AD Diagnostic					
Autopsy	-	29 (19.6%)	11 (36.7%)	40 (22.5%)	
PET	-	1 (0.7%)	1 (3.3%)	2 (1.1%)	**0.047**
CSF	-	118 (79.7%)	18 (60.0%)	136 (76.4%)	

*Summary statistics for historical controls are included for reference but not tested in statistical comparisons as subject level data was unavailable. *p* values refer to pairwise comparisons between LBD-AD and LBD+AD only.

Figure 1: Hippocampal Volume and Adjacent Cortical Thickness



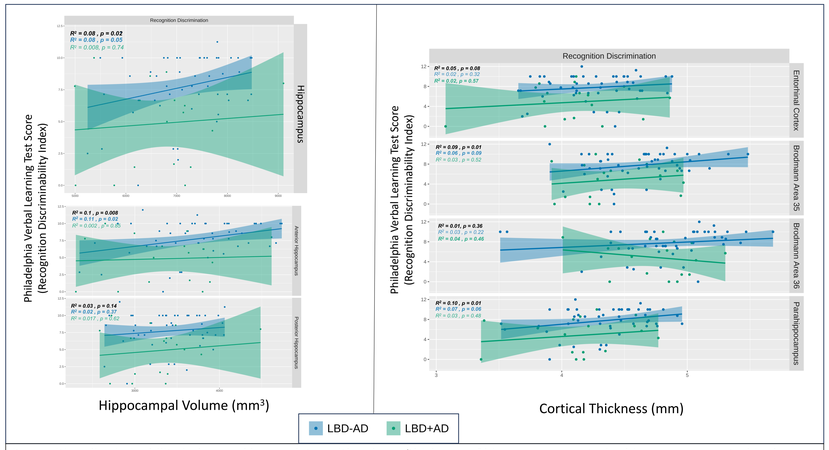
Uncorrected pairwise comparisons show greater atrophy in LBD+AD compared to LBD-AD in anterior hippocampus, Brodmann area 35 and parahippocampus. Volume and thickness measures are adjusted for age, sex, and intracranial volume. Historical controls' summary statistics were based upon a previously reported cohort[3].

Table 2: Hippocampal Measures and Group Comparisons

	Control* (N=190)	LBD-AD (N=148)	LBD+AD (N=30)	*p* value (adjusted)	Cohen's *d*
Hippocampal Volume [SD] (mm³)	6742.0 [618.0]	7090 [792]	*6826 [891]*	*0.078 (0.104)*	*0.370*
Anterior Hippocampus [SD] (mm³)	3449.0 [451.2]	3687.3 [541]	3470.6 [518]	**0.040 (0.093)**	**0.433**
Posterior Hippocampus [SD] (mm³)	3293.0 [320.2]	3402.4 [378]	3355.2 [429]	0.502 (0.502)	0.141
Entorhinal Cortex [SD] (mm)	4.04 [0.323]	4.19 [0.318]	*4.08 [0.365]*	*0.089 (0.104)*	*0.358*
Brodmann Area 35 [SD] (mm)	4.70 [0.321]	4.69 [0.348]	**4.52 [0.407]**	**0.024 (0.084)**	**0.476**
Brodmann Area 36 [SD] (mm)	4.82 [0.428]	*4.89 [0.394]*	*4.76 [0.401]*	*0.086 (0.104)*	*0.362*
Parahippocampus [SD] (mm)	4.30 [0.280]	4.34 [0.314]	**4.17 [0.402]**	**0.012 (0.084)**	**0.530**

All LBD measures were adjusted for age, sex, and intracranial volume. *p* values and effect sizes refer to pairwise comparison between LBD-AD and LBD+AD and are uncorrected for multiple hypothesis testing. p value adjusted for multiple hypotheses is in parenthesis.

Figure 2: Verbal Memory Performance



Recognition discriminability index weakly correlates with volume/thickness of hippocampus, anterior hippocampus, entorhinal cortex, Brodmann area 35 and parahippocampus (p-values unadjusted for multiple comparisons). No difference in effects are seen among LBD-AD and LBD+AD.

Conclusion

- LBD+AD trends toward greater hippocampal atrophy relative to LBD-AD.
- Among all LBD, hippocampal volume has a weak positive correlation with verbal memory performance.
- However, the correlation between hippocampus and memory measures does not significantly differ in the presence of AD-copathology.
- Thus, non-AD mechanisms may contribute to the correlation of hippocampal volume and verbal memory in LBD.

References

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