



Mechanistic Insights into Processes Driving Neurodegeneration and Cognitive Impairment in Lewy Body Dementia

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INTRODUCTION

- Lewy body dementia (LBD) is the second most common neurodegenerative dementia after Alzheimer's disease¹.
- LBD includes Parkinson's disease dementia (PDD) and dementia with Lewy bodies (DLB)².
- LBD is characterised by the accumulation of α -synuclein into Lewy bodies².
- Iron accumulation has been linked to cognitive impairment in Parkinson's disease³.
- Excess iron promotes oxidative stress and neuronal damage.
- The mechanisms underlying neuronal loss and cognitive decline in LBD remain unclear.

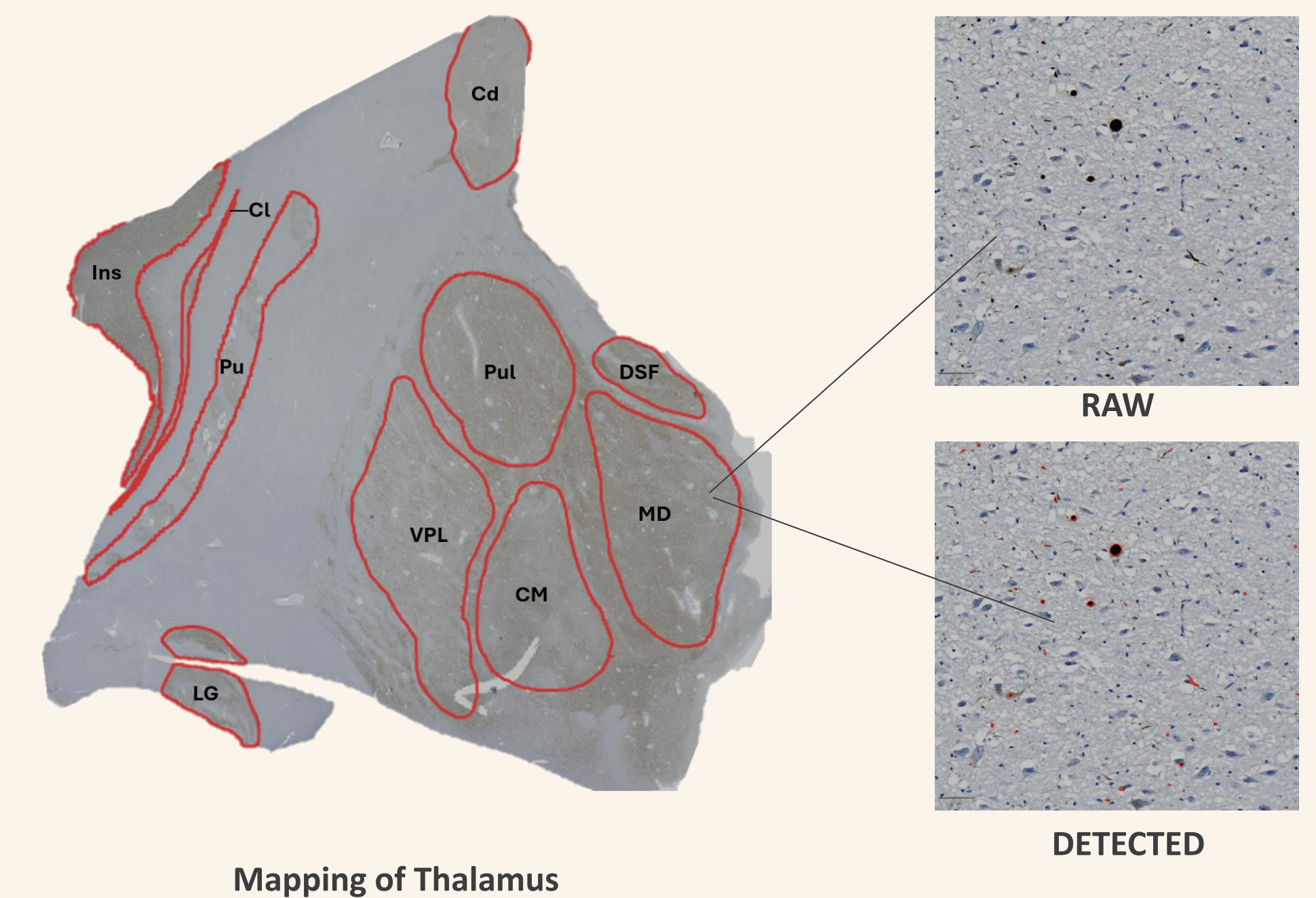
PROJECT AIMS

- Characterise the relationships between LBD pathology, neuronal loss, co-pathologies, and cognitive decline.
- Determine whether iron accumulation and oxidative damage contribute to neuronal loss independently of Lewy body pathology.
- Evaluate 7T MRI markers of brain iron and their association with clinical outcomes in LBD.

METHODS

Protein Pathology Analysis

- 19 cases : Control (n=5), MCI-LB (n=4), DLB (n=5), ILBD (n=5).
- Thalamic sections immunostained for phosphorylated α -synuclein.
- 3 cases excluded due to absence of the mediodorsal thalamic nucleus.
- Protein pathology quantified in QuPath as % area immunopositivity in the Mediodorsal (MD) nucleus of thalamus.
- Group comparisons performed in GraphPad Prism using Welch's t-test.

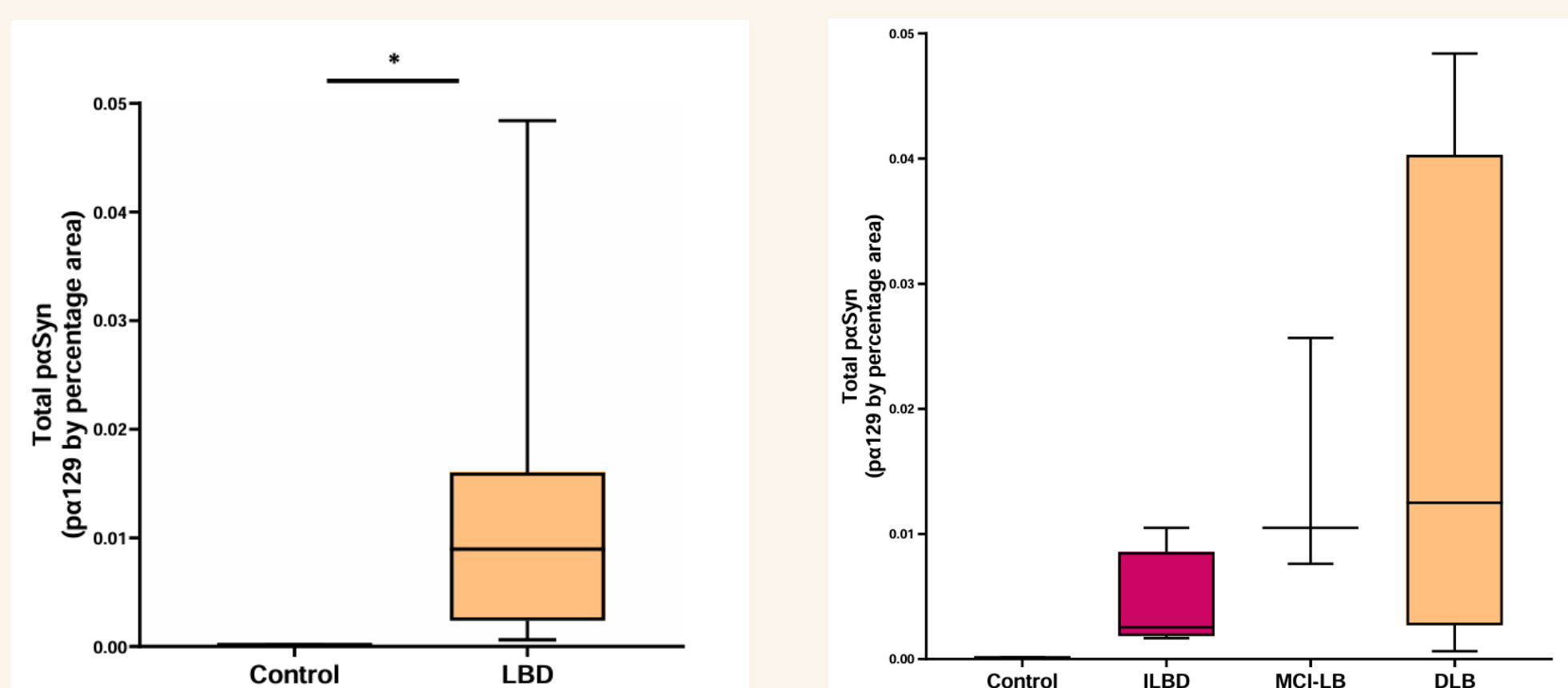


RESULTS

Group level comparisons of α -synuclein

Significant group level differences of α -syn observed.

- Variation in pathology throughout LB disease spectrum.



DISCUSSION & FUTURE WORK

- α -syn pathology is associated with disease stage in MD nucleus.
- Larger cohort size is required to increase power and significance.
- Tau, amyloid- β analysis and correlation in expanded cohort.
- Neuronal count using MAP2 to quantify neuronal loss.
- Perls and Turnbull's stain for iron abundance in MD.

