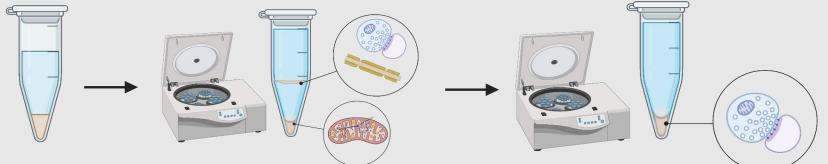
What is Dementia with Lewy Bodies?

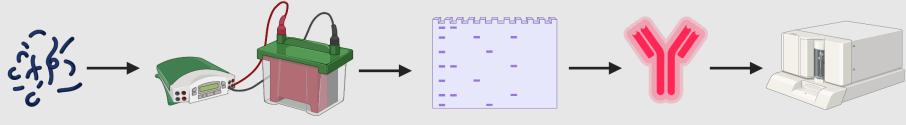
Mitochondrial Abnormalities In Dementia with Lewy Bodies

Dementia with Lewy bodies (DLB) is a common form of memory loss in elders ⁽¹⁾. DLB is characterised pathologically by the accumulation of α -synuclein protein⁽²⁾ that aggregates to form abnormal deposits called Lewy Bodies⁽³⁾ in cortical brain regions, resulting in the clinical symptoms of DLB. Symptoms: REM sleep behavioural disorder Memory Loss Parkinsonism Hallucinations **Affected Neuron:** Lewy Bodies can affect different areas of the brain : Cerebral cortex responsible for information processing • Limbic cortex responsible for emotion and behaviour • Hippocampus, essential for the formation of new memories Midbrain for control of movement Lewy Body *All images are taken from Biorender Methods *All images are taken from Biorender

1. Homogenization of tissue & centrifugation at 1.300rcf to obtain Pellet 1 Nuclei



- 2. Mix 50:50 24% Percoll and layer
- 3. Centrifugation at 25,000rcf to obtain Mitochondria & Synaptosomes



- 4. Proteins denatured in LDC sample loading buffer
- 5. Samples run on 4-12% precast polyacrylamide gel

6. Samples transferred onto nitrocellulose membrane & probed with monospecific antibodies to protein of interest; Visualized using near-infrared fluorescent detection (LI-COR)

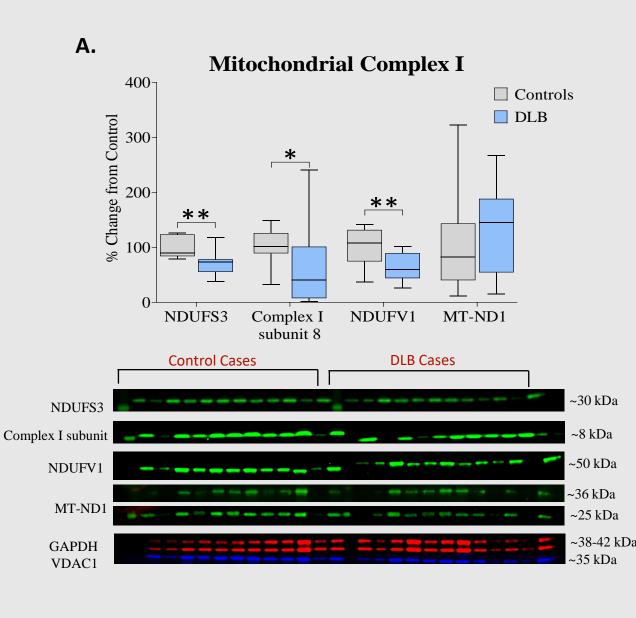
Aims

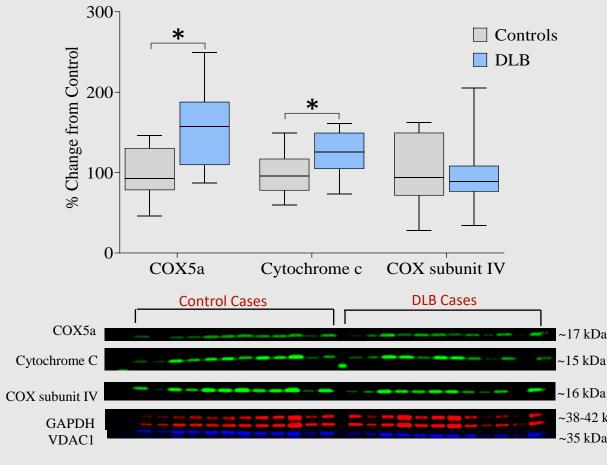
The aim of this project was to test if the symptoms of DLB are due to a build-up of α -synuclein in neuronal synapses, which cause damage to neuronal cells.

Hypothesis

Results

D.





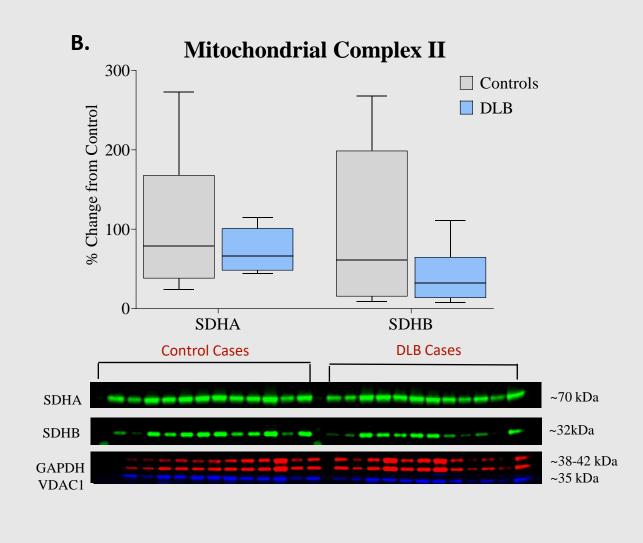
Conclusion

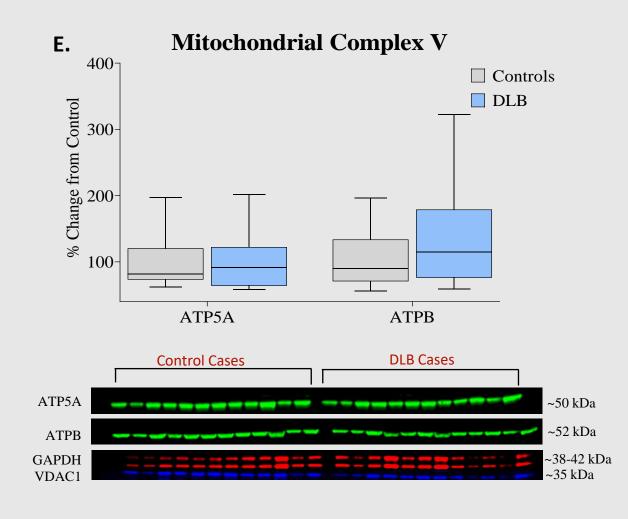
We have developed a simple method for the isolation of highly enriched mitochondria from post-mortem human brain. This has enabled us to show:

- Relatively selective decrease in the expression of Complex I subunits in DLB, similar changes to that observed in Parkinson's Disease.
- No change in nuclear encoded Complex II subunits, indicating possible mitochondrial DNA damage to Complex I subunits.
- Increase in specific Complex III and Complex IV subunits. May be a compensation for decreased Complex I activity.

Mitochondrial activity are significantly altered in DLB and may explain some of the altered brain metabolism seen using neuroimaging in patients. Further investigation of mitochondrial activity in DLB is therefore warranted, along with determination of mitochondrial DNA damage.

Metabolic abnormalities are frequently seen using neuroimaging methods in key brain areas in DLB patients. We hypothesize this is due to mitochondrial changes controlling cellular respiration.





Mitochondrial Complex IV

References

1. McKeith I. Dementia with Lewy bodies. Dialogues Clin Neurosci. 2004;6:333-341. 2. Outeiro TF, Koss DJ, Erskine D, Walker L, Kurzawa-Akanbi M, Burn D, Donaghy P, Morris C, Taylor JP, Thomas A, et al. Dementia with Lewy bodies: an update and outlook. Mol Neurodegener. 2019;14:5. 3. Ageing N-NIo. What Is Lewy Body Dementia? Causes, Symptoms, and Treatments. 2021 [cited 2023 13 July].

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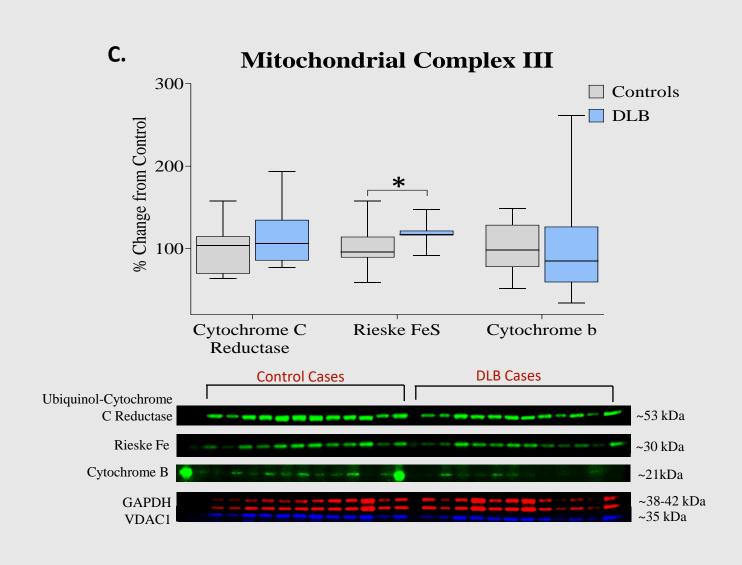


Figure 1. Mitochondrial Protein Determination in Isolated Human Brain Fractions

Mitochondrial proteins were determined using monospecific antibodies and western blotting to demonstrate A. Complex I, B. Complex II, C. Complex III, D. Complex IV, and *E*. Complex V.

Results are expressed as a ratio of specific protein compared to mitochondrial VDAC1 protein as a loading control.

* = p-value is less than 0.05

** = p-value is less than 0.01

