

Visual Hallucinations in patients with Dementia with Lewy Bodies

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Introduction

- Dementia with Lewy Bodies (DLB) is the second most common cause of Dementia with Alzheimer's disease the most, it is responsible for 150,000 dementia cases out of 800,000 dementia sufferers within the UK.
- Around 70% of patients suffer from intense visual hallucinations which can be extremely distressing.
- Lewy Bodies are inclusions which are found within nerve cells in the brain and are made up of Alpha-Synuclein clumping together to form an aggregate. Alpha-Synuclein is found at the tips of cells and are involved in the transfer of messages from neuron to neuron.
- DLB is still little understood but it is thought that damage to the visual system (figure 3) in the brain is the cause of the hallucinations. In particular the Inferior Temporal Gyrus and the Fusiform Gyrus which are thought to be associated with the brains ability to recognise objects, faces, etc.

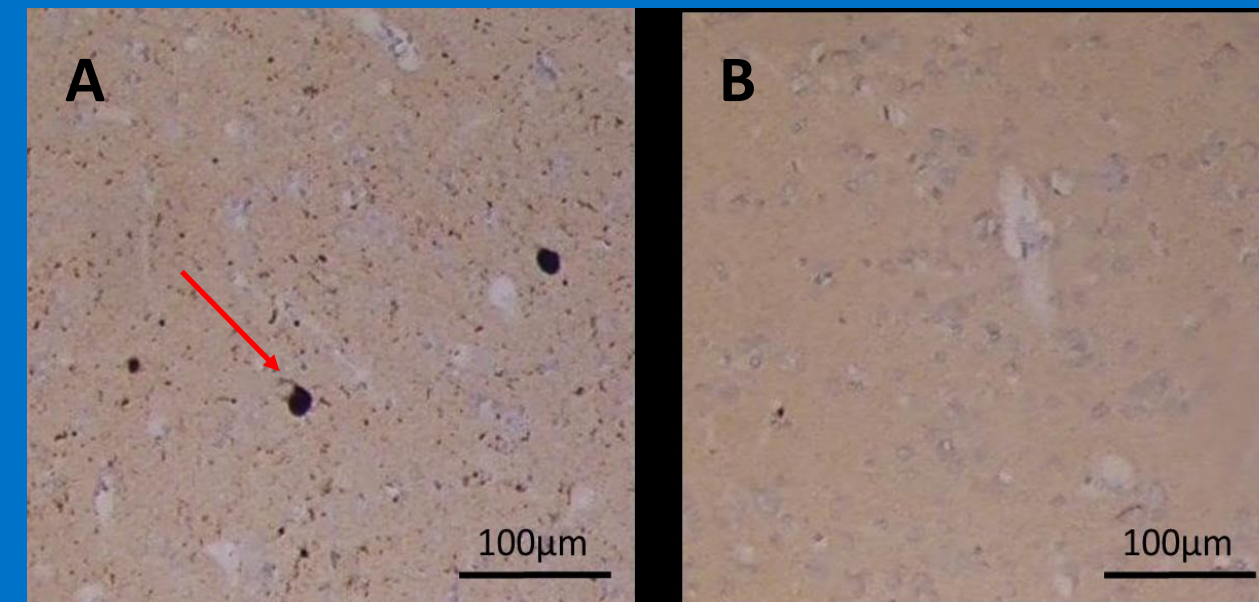


Figure 1: DLB and age matched brains. The red arrow in A shows such an aggregate as compares to a age

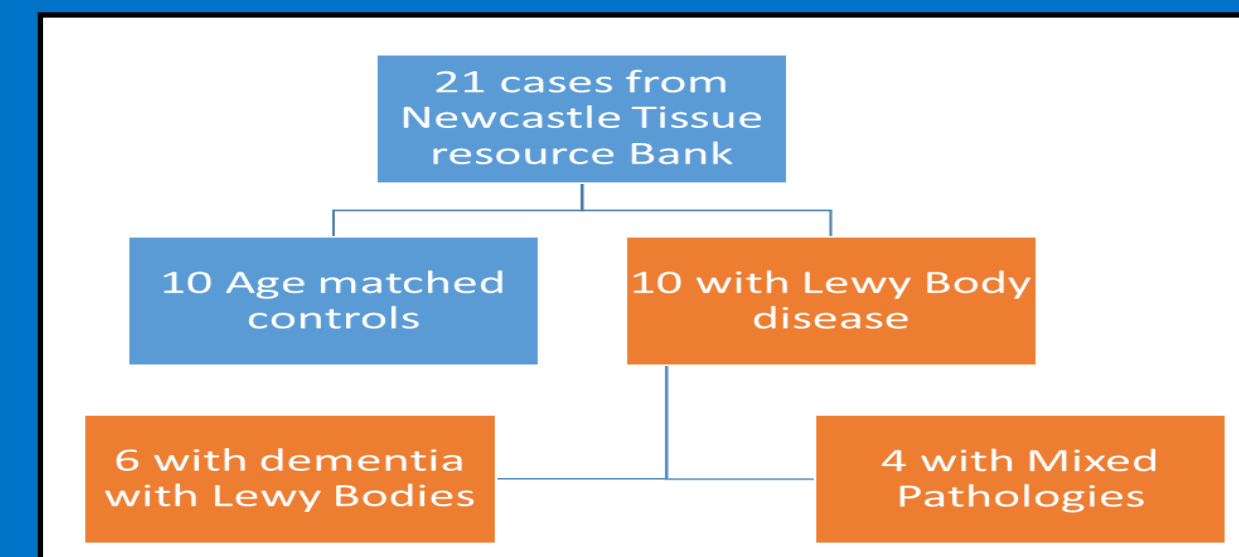


Figure 2: shows the breakdown of the 21 cases used in the experiment, orange squares indicates that the patient had Visual Hallucinations during life

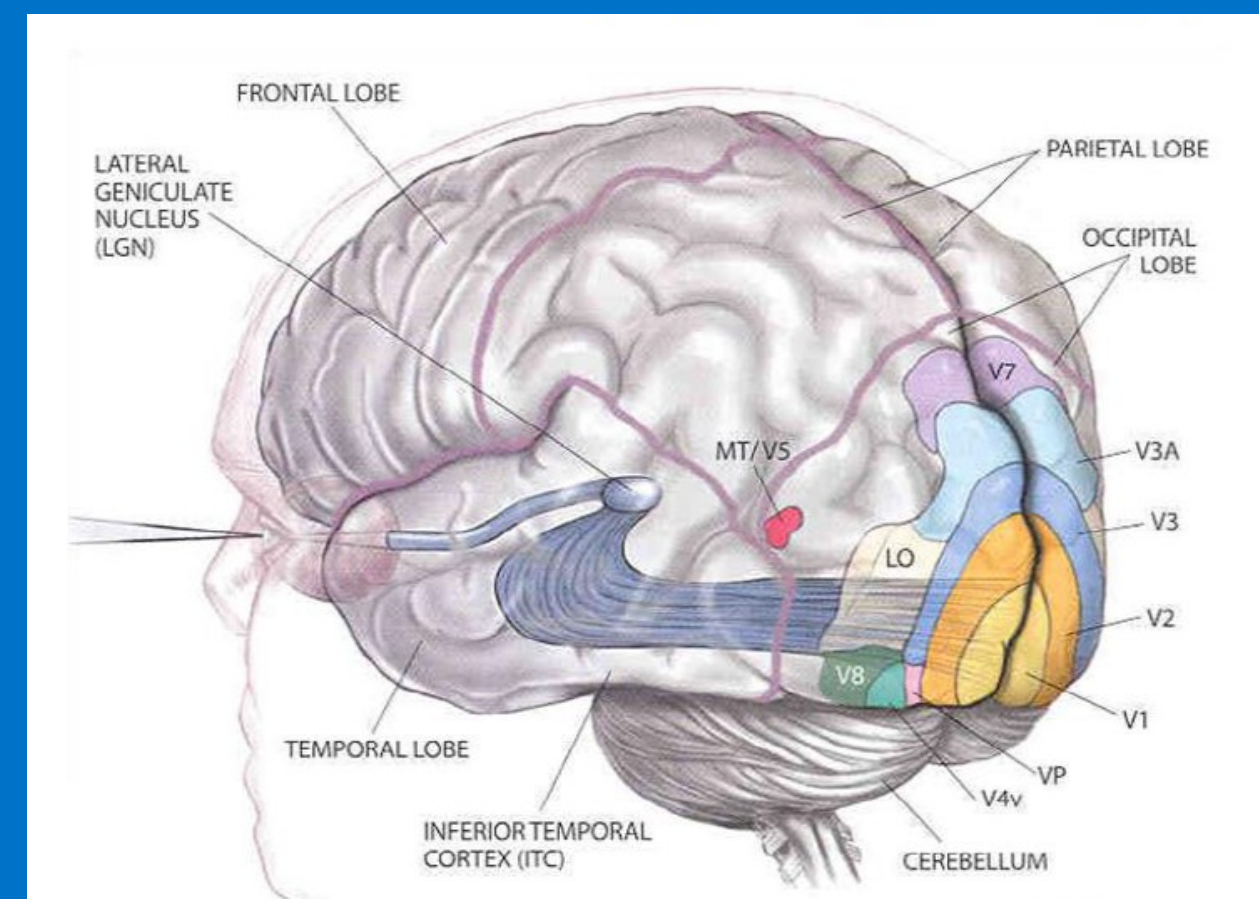
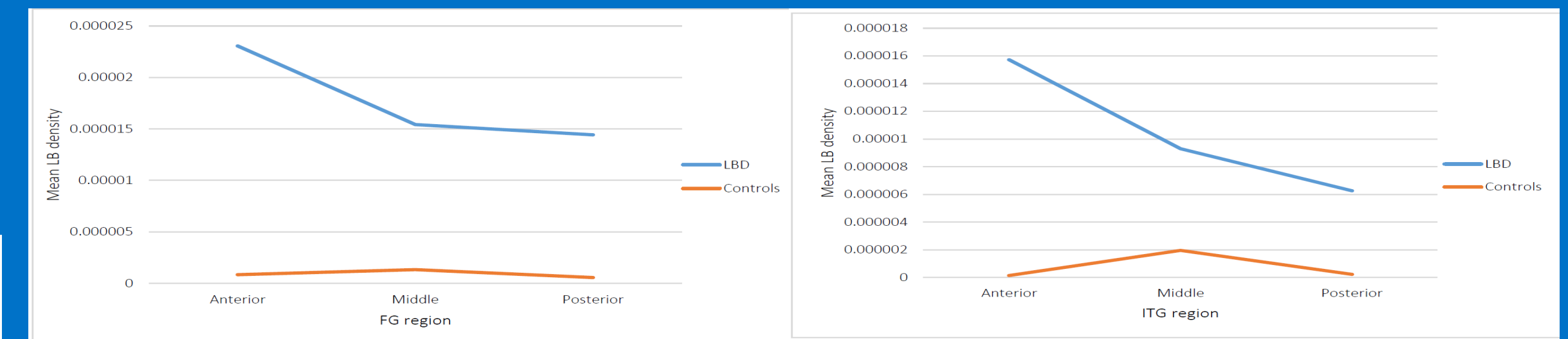


Figure 3: shows the position of the Primary visual cortex in the occipital lobe of the brain where input from the eyes is first processed before being passed to the ITG and Fusiform Gyrus.

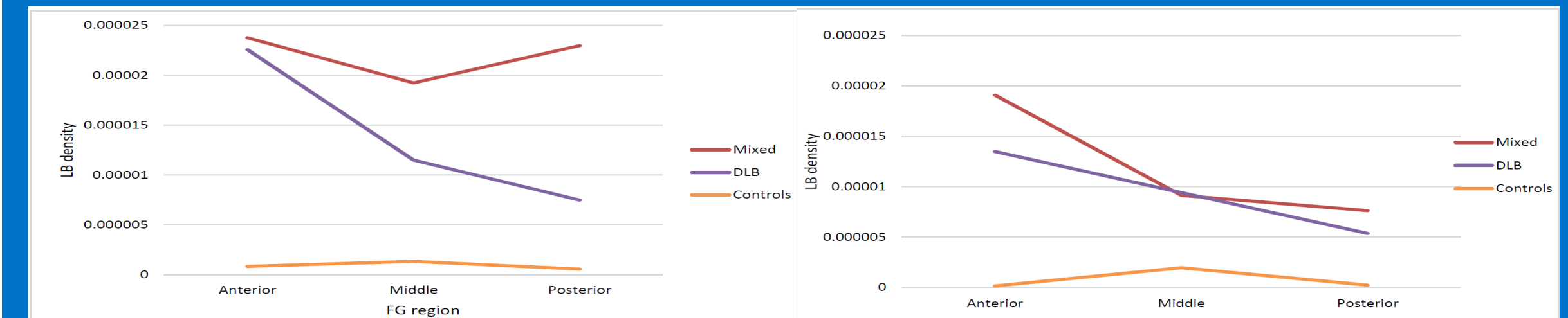
Results

- Images were then randomly taken from the ROIs with the use of a computer programme and these were analysed to quantify the number of Alpha-Synuclein aggregates per slide.
- For both the Fusiform Gyrus and the Inferior Temporal Gyrus there was a significant difference found between the Lewy Body density in those that had Dementia with Lewy Bodies and the controls.
- Lewy Bodies can be found in normal elderly brains where the patient may not have experienced any Lewy Body disease. So to prove that this was the cause of dementia with Lewy Bodies graphs 1 and 2 show that there is a significantly higher density of Lewy Bodies in cases with Lewy Bodies disease than those without.
- Interestingly the anterior (or front) of the gyri had higher Lewy Body (LB) density than either the middle or posterior. This could suggest that the anterior of each Gyri are important in Lewy Body Disease.
- However, not all the Lewy Body Disease cases suffered from just dementia with Lewy Bodies as we also had some mixed pathology cases in there as well (figure 2).
- Graphs 3 and 4 breakdown the results to show that the pattern of the anterior having higher LB density hold true amongst Dementia with Lewy bodies cases but not with the mixed pathologies.



Graph 1: Mean LB density in the anterior, middle and posterior portions of the FG in LBD cases and con-

Graph 2: Mean LB density in the anterior, middle and posterior portions of the ITG in controls and LBD.



Graph 3: Mean LB density in the anterior, middle and posterior portions of the FG across three cohorts.

Graph 4: Mean LB density in the anterior, middle and posterior portions of the ITG across three cohorts.

Conclusions

- The results we obtained appear to support the current thinking that a problem with Alpha-Synuclein creating Lewy Bodies is behind the visual hallucinations some patients suffer from.
- The experiment also suggests that both the Fusiform gyrus and the Inferior Temporal Gyrus play a role in this due to the high levels found within both these structures involved in object recognition.
- We also found out that there is a particular increase in the Lewy Body density within the anterior part of each structure which could lead to a development in our understanding of the pathophysiology of the disease.

Samples

- 21 samples were used, ten cases had Lewy body disease and had experienced Visual hallucinations during life however 6 cases had only been diagnosed with Dementia with Lewy Bodies and 4 had symptoms for other possible causes of dementia as well. The other ten were normal brains from age matched samples to allow comparison. All of the brains are cut into standardised blocks so as to make comparison possible.

Slicing

- A sharp razor on a Microtome is used to create thin 10µm or 30µm and placed on glass slides
- By taking multiple slices from the blocks we were able to look at the Anterior, Middle and Posterior of each Gyrus.

Staining

- These are then stained with an antibody (5G4 anti-Alpha-Synuclein). This then works by binding to Alpha-Synuclein and allows the abnormal aggregations to be seen.

Delineation

- However, we are not interested in the entire block so we then need to locate the regions of interest (ROI) which in this case are the Inferior Temporal Gyrus and the Fusiform Gyrus. This was done by using a brain atlas which shows cross sections of the brain and which gyri are located in each part.