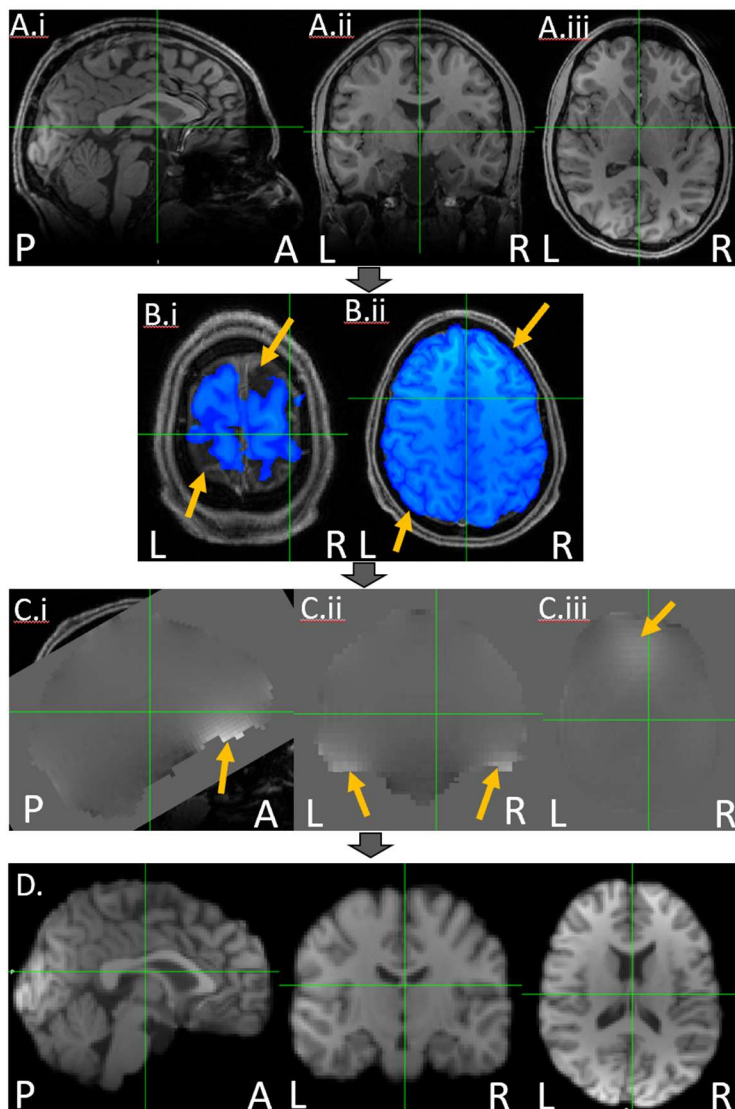


## MRI Scans Show Grey Matter Loss in the Hippocampus and Amygdala in Alzheimer's Disease patients.

### MRI Pre-processing steps



*Figure 1 - MRI pre-processing Steps Flowchart*

**Figure 1A: First step of MRI pre-processing: Original T1 Magnetic Resonance Imaging (MRI) scan (Siemens 3.0T magnet) of a young healthy adult's head.** MRI creates high resolution *in vivo* images through magnetic fields and radiowaves. It is used to investigate changes in function or morphology, as well as any abnormalities. Images need to go through pre-processing steps to correct signal distortion, motion correction, and spatial smoothing to increase the ratio of signal to noise. A.i) Sagittal view of original scan, posterior side of the head on the left side of the image (P), anterior side on the right (A). A.ii) Coronal view, left side of the head on the left (L), right side on the right (R) for neurological orientation. A.iii) Axial view.

**Figure 1B: Second MRI pre-processing step: Brain extraction tool (BET) identifying brain tissue and cerebrospinal fluid (CSF) amidst a whole-head MRI scan.**

Blue region is what BET extracted as brain tissue and CSF. This step is

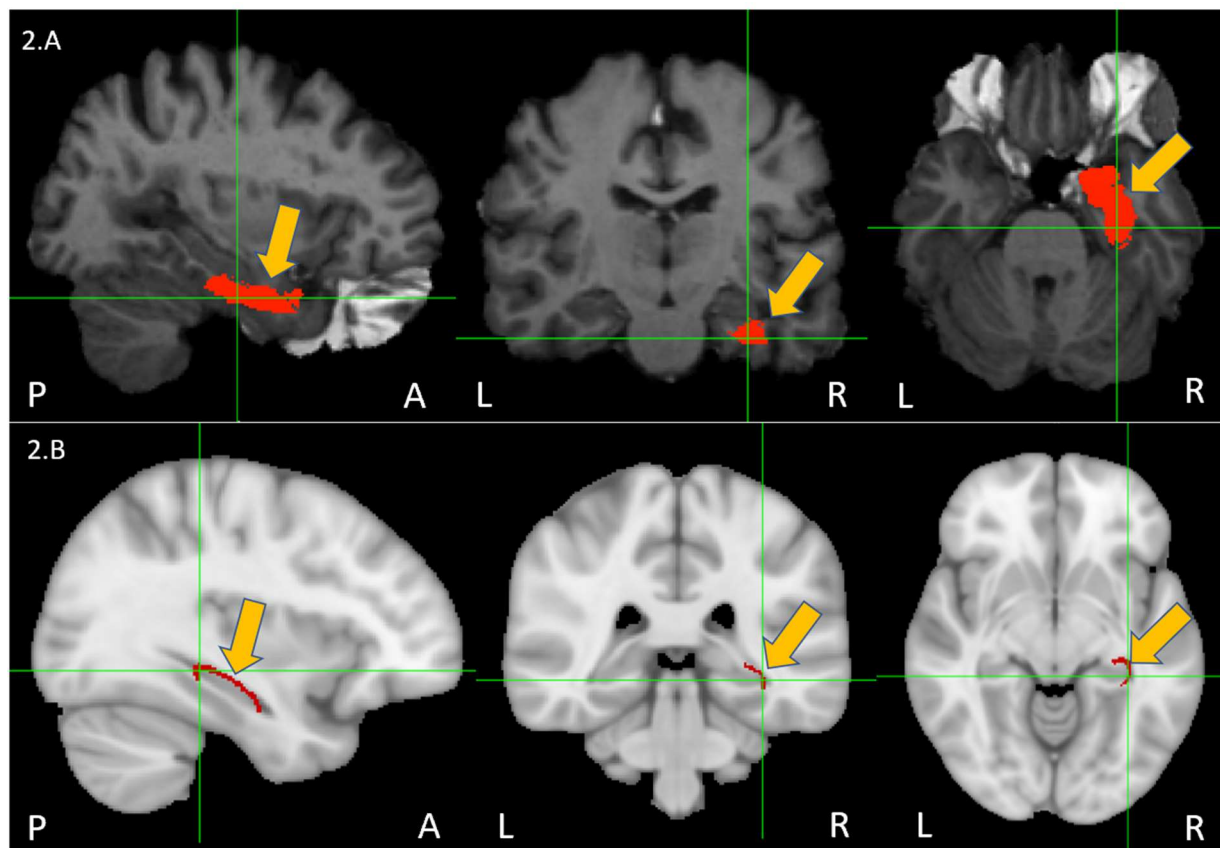
necessary to improve accuracy of brain volume measures and other quantitative analyses. B.i) Example of BET not accurately extracting brain tissue, yellow arrows point to brain parts BET missed. B.ii) Example of BET accurately extracting brain tissue, yellow arrows point to accurately extracted parts of the brain compared to Fig1B.i. B.i and B.ii both show the brain from an axial view.

**Figure 1C: Third MRI pre-processing step: Fieldmap processing to identify areas with high signal distortion.** This works by measuring the magnetic field intensity across space. Yellow arrows across all three planes show the white areas indicating most signal variation. These areas have the most changes in tissue interface, making the signal inhomogeneous. Fieldmap

processing is used to identify areas that need algorithms to correct distortions to make images more accurate. Fig1C.i and 1C.iii show arrows pointing to the prefrontal cortex. Fig1C.ii arrows point to inferior temporal lobes.

**Figure 1D: Last pre-processing step: Standardization of subject's scan with MNI152 by FEAT GUI.** The image is blurry compared to the high-resolution scan as MNI152 consists of 152 registered healthy standardized brains, making the image blurry as each voxel is stretched on all three planes to fit a mask which has been standardized between these 152 brains, making the image lose resolution. This is needed to compare scans or determining coordinates. The scan is now ready for accurate analysis after being processed in standard space and corrected for artefacts like signal distortion.

### Shape and volumetric analysis of Alzheimer's disease patients

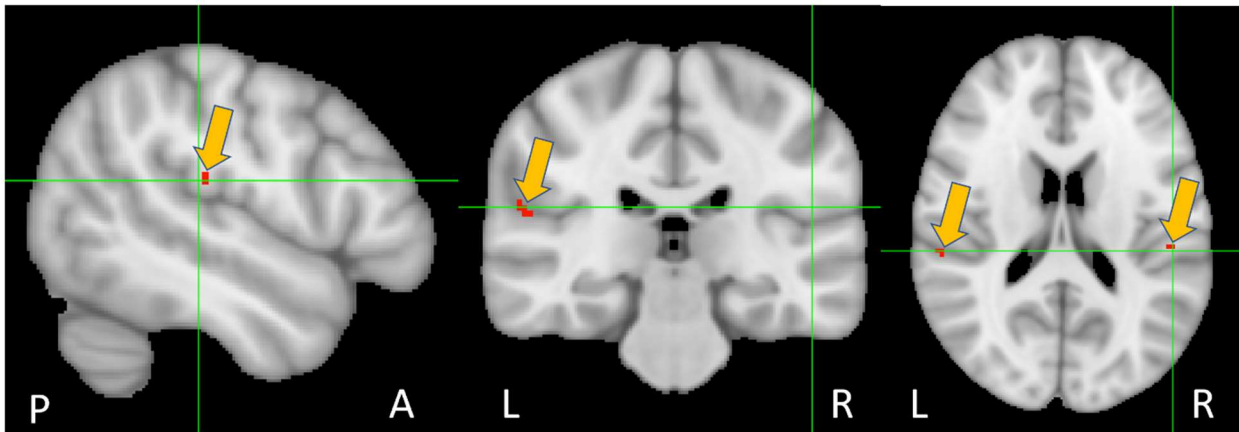


*Figure 2 – Shape analysis of hippocampus and amygdala in Alzheimer's disease patients vs. healthy controls*

**Figure 2A: Segmentation mask of hippocampus and amygdala on T1 MRI scans (Siemens 3.0T) of one healthy control (age-matched to Alzheimer's disease (AD) patients).** Left (L) and right (R) indicate neurological orientation. MRI scan is standardized as it is already

preprocessed. Yellow arrows in all three planes indicate the hippocampus-amygdala segmentation mask.

**Figure 2B: Structural differences in the hippocampus and amygdala of 3 severe AD patients compared to 5 age-matched healthy controls.** Yellow arrows in all three planes point to the shape differences between the two groups. This is where the location differences of vertices are significant between AD patients and the healthy control group.



*Figure 3 – Volumetric analysis with Voxel-Based Morphometry (VBM) of AD patients vs healthy controls*

**Figure 3: Volumetric analysis with Voxel-Based Morphometry (VBM) of 8 mild-to-moderate AD patients vs 10 healthy age-matched controls amygdala on T1 MRI scans (Siemens 3.0T).** MRI images were already processed with standardization and applied a mask specific to grey-matter. L and R indicate neurological orientation. Yellow arrows point to areas where VBM detected grey matter tissue loss in AD patients based on control group. MNI coordinates of chosen cluster are [140, 98, 90].

## Discussion

Figure 2B shows areas where AD patients have shape differences in the hippocampus and amygdala compared to healthy age-matched controls. To know whether these structural changes are caused by grey-matter tissue loss, a volumetric analysis was conducted in figure 3 where VBM detected differences in grey matter volume in certain regions. These analyses demonstrated the differences in shape of the hippocampus and amygdala to be due to a reduction in grey matter volume in AD patients. This was supported by control groups having greater grey-matter volume in the regions shown. Moller et al.'s 2014<sup>1</sup> study supports these findings, though Fjell et al.'s 2014 study also mentions that loss of hippocampal volume is part of normal aging<sup>2</sup>.

## References

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