Impact of Variability in Brian Volume Measurements from MRI scans in Multi- Centre Neurodegeneration Assessments

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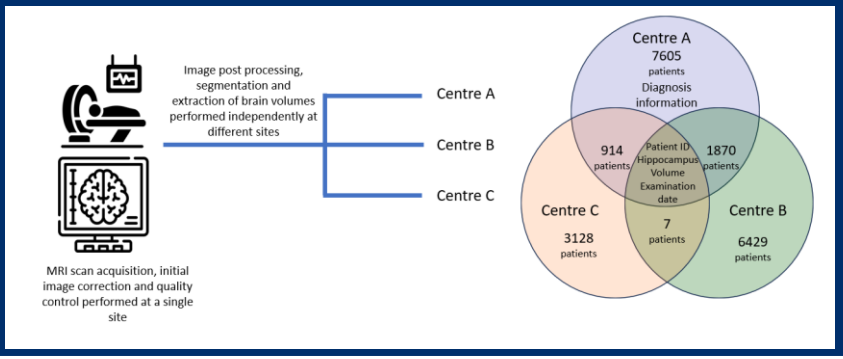
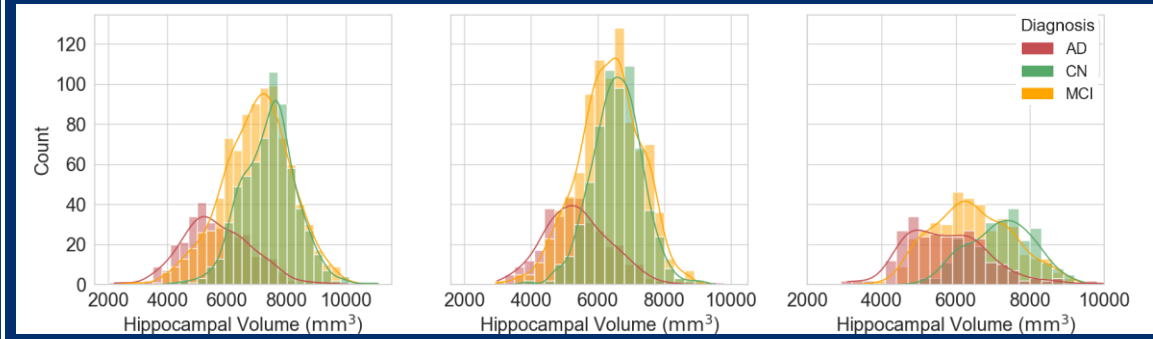
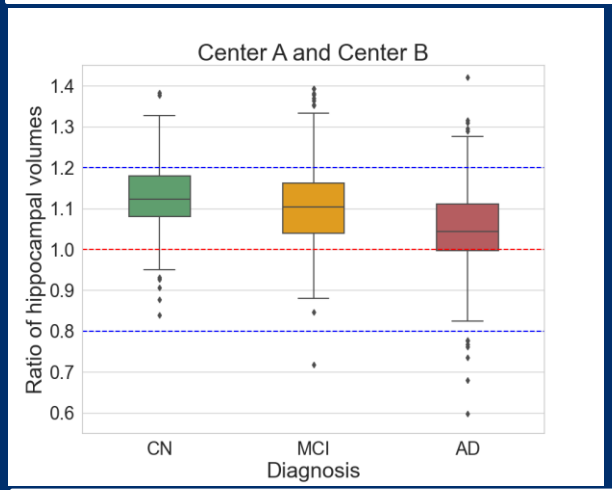


Fig 1: MRI scans were acquired at one centre where preprocessing image corrections were performed. Post processing including image segmentation and brain volume extraction was performed at three different centres. Centre A (middle n = 1870), centre B (right n = 1870), centre C (left n = 914)

Fig 3: Distribution of hippocampal volumes at each centre when separated by diagnoses was found to be non-normal as per Anderson Darling statistical tests. Mann Whitney U tests between centres show that there are **statistically significant differences between the distribution of hippocampal volumes for each of the diagnoses between centres**. Centre A (left n = 1870), centre B (middle n = 1870), centre C (n = 914)



Degree of neurodegeneration [1]	Mild	Moderate	Severe
Hippocampal Shrinkage	5 %	12 %	34%



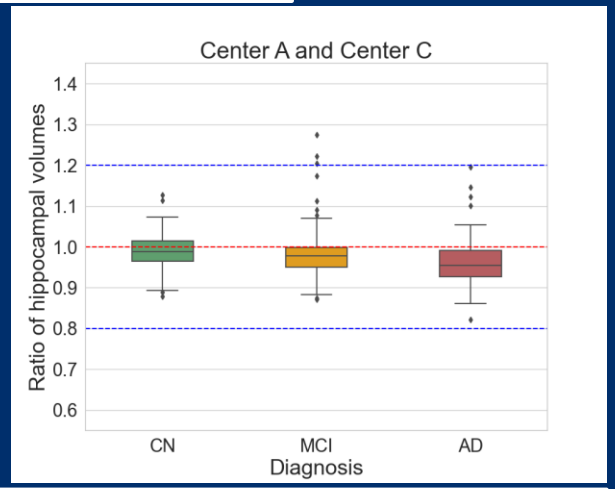


Fig 2: Hippocampal volumes recorded at Centre A were larger than those recorded at Centre B in 88 % of the cases (n = 1870). Hippocampal volumes recorded at Centre A were smaller than those recorded at Centre C in 74 % of the cases (n = 914). The blue lines indicate 20 % difference in hippocampal volumes between the centres. **These differences are due to a lack of standardization in image processing pipelines and image processing analyses in different centres.** Centre A vs Centre B (left), centre A vs centre C (right).

Diagnosis (Centres, sample size)	Patients exceeding threshold for mild dementia	Patients exceeding threshold for moderate dementia	Patients exceeding threshold for severe dementia	Patients not exceeding any threshold
CN (A v B, n=646)	270 (42 %)	286 (44 %)	0 (0 %)	90 (14 %)
MCI (A v B, n=898)	324 (36 %)	332 (37 %)	1 (0 %)	241 (27 %)
AD (A v B, n=326)	113 (35 %)	69 (20 %)	3 (1 %)	141 (43 %)
CN (A v C, n=258)	52 (20 %)	2 (1 %)	0 (0 %)	204 (79 %)
MCI (A v C, n=390)	112 (29 %)	11 (3 %)	0 (0 %)	267 (68 %)
AD (A v C, n=266)	106 (40 %)	25 (9 %)	0 (0 %)	135 (51 %)

Table 1: The table shows the number of patients at risk of inconsistent diagnoses based on measurements at different centres of the same (standardised) timepoint scan using thresholds for neurodegeneration progression [1]. This difference is solely due to the difference in data processing and analyses pipelines between the centres. **The lack of standardisation reduces confidence in longitudinal measurements risking patient misdiagnoses and will negatively impact treatment**

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[1] Vijayakumar, A. and Vijayakumar, A., 2013. Comparison of hippocampal volume in dementia subtypes. *International Scholarly Research Notices*, *2013*(1), p.174524.

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