

## Introduction

The aim of this research is to investigate measurable differences between normal cognition (CN) and mild cognitive impairment (MCI) through multimodal imaging. To investigate this, we selected 160 subjects (normalized for age, education and gender) from the Alzheimer's Disease Neuroimaging Initiative (ADNI) [1] dataset who have received all forms of required imaging.

We investigate the effectiveness of rs-fMRI, dMRI and multi modal classification on a quality controlled subject cohort. We hypothesized that fusion of rs-fMRI and dMRI would provide a more complete picture of a subjects cognitive health, providing increased classification performance.

## Methods

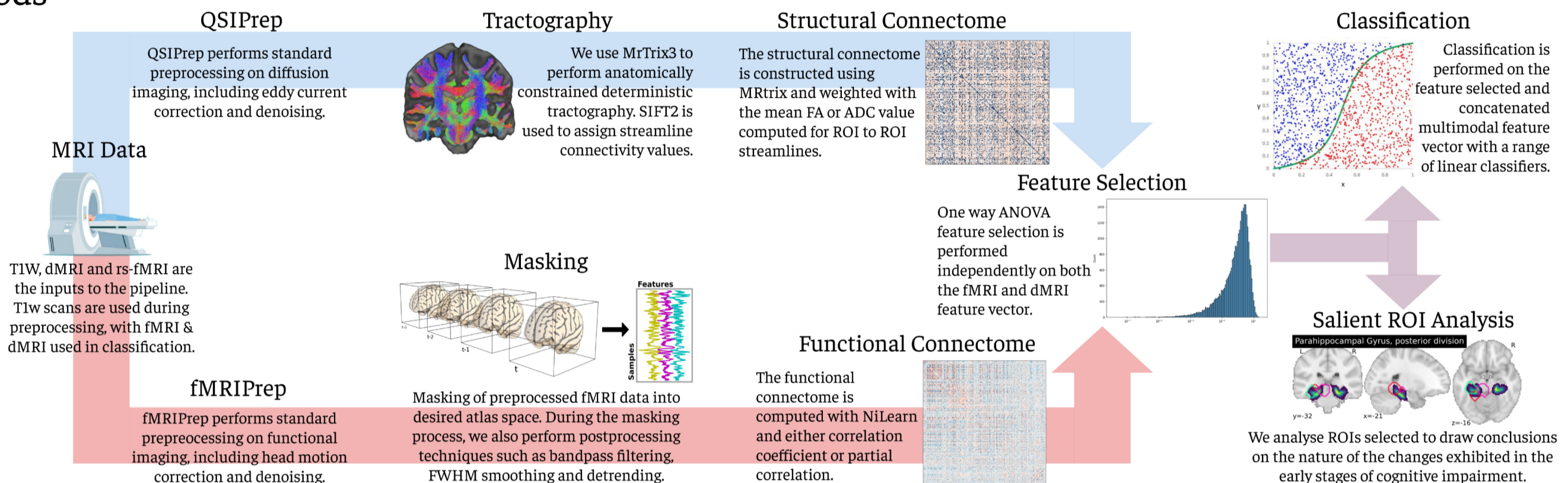


Figure 1: Summary diagram of the experimental pipeline from data acquisition to classification and analysis.

## Results

Our investigation showed that multimodal imaging data can provide statistically significant increases in AUC for classifying MCI vs CN patients. Our peak accuracy of 0.73 AUC shown in Table 1 was validated through 10 fold cross validation across 3 random seeds.

We found that the HCP 300 ICA atlas performed optimally in multimodal classification, aligning with Dadi et al. recommendations on optimal atlas dimensionality [2]. Mean diffusivity outperforming fractional anisotropy for structural connectome weighting aligns with previous literature consensus [3], with increased mean diffusivity being a potentially strong discriminator between CN and MCI subjects. Figure 2 shows a summary of our hyperparameter exploration via grid search.

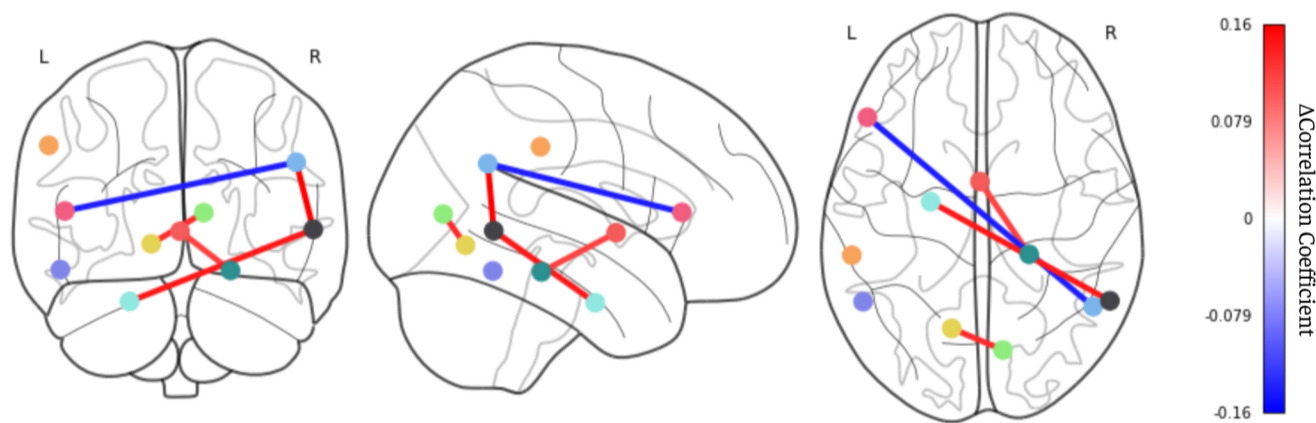


Figure 3: Connectivity difference between CN and MCI population means for salient ROIs identified by feature selection analysis

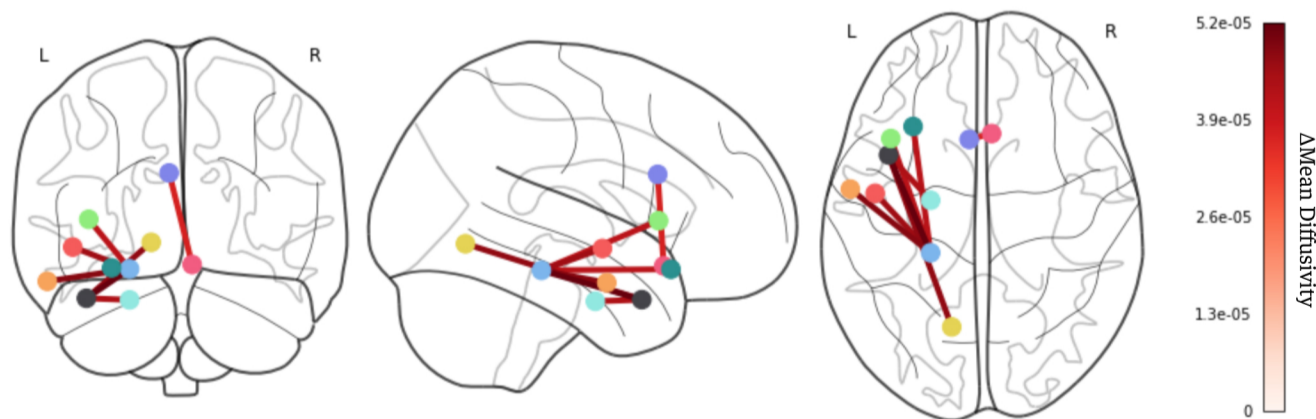


Figure 4: Mean diffusivity difference between CN and MCI population means for salient ROIs identified by feature selection analysis

## Conclusions

We explored a multimodal approach to the diagnosis of MCI, proving our method of combining functional connectivity and mean diffusivity measures through feature-level fusion to be greater than the sum of its parts, significantly improving the results achieved by either modality in isolation. We found that our approach performed optimally when the features constructed from each modality were unlikely to contain much informational overlap; achieved by using atlases with contrasting construction methods & region definitions. Furthermore, we showed that aggressive feature selection methods are important to improving diagnostic results and conducted two separate analyses into selected regions and connections from the functional and structural feature sets.

## References

- [1] Mueller, S.G., Weiner, M.W., Thal, L.J., Petersen, R.C., Jack, C., Jagust, W., Trojanowski, J.Q., Toga, A.W. and Beckett, L., 2005. The Alzheimer's disease neuroimaging initiative. *Neuroimaging Clinics of North America*, 15(4), p.869.
- [2] Dadi, K., Varoquaux, G., Machlouzarides-Shalit, A., Gorgolewski, K.J., Wassermann, D., Thirion, B. and Mensch, A., 2020. Fine-grain atlases of functional modes for fMRI analysis. *NeuroImage*, 221, p.117126.
- [3] Stebbins, G.T. and Murphy, C.M., 2009. Diffusion tensor imaging in Alzheimer's disease and mild cognitive impairment. *Behavioural neurology*, 21(1, 2), pp.39-49.
- [4] Chan, D., Fox, N.C., Schill, R.I., Crum, W.R., Whitwell, J.L., Leschziner, G., Rossor, A.M., Stevens, J.M., Cipolletti, L. and Rossor, M.N., 2001. Patterns of temporal lobe atrophy in semantic dementia and Alzheimer's disease. *Annals of neurology*, 49(4), pp.433-442.
- [5] Wang, K., Liang, M., Wang, L., Tian, L., Zhang, X., Li, K. and Jiang, T., 2007. Altered functional connectivity in early Alzheimer's disease: A resting state fMRI study. *Human brain mapping*, 28(10), pp.967-978.

Functional Atlas	Structural			AUC			
	Conf.	Conn.	K				
Schaefer100x7 <sup>a</sup>	CC	Partial Corr.	64	—	0.6722		
	—			Schaefer100x7 <sup>a</sup>	MD	128	0.6625
HCP300	CC	Corr.	32 <sup>b</sup>	Craddock249	MD	16 <sup>b</sup>	<b>0.7319</b>

Table 1: Best performing hyperparameters for functional, structural and multimodal.

<sup>a</sup> Both functional and structural features are mapped to the Schaefer100x7 atlas

<sup>b</sup> Significantly lower values of K are optimal for the multimodal approach

'CC' refers to CompCor confound removal

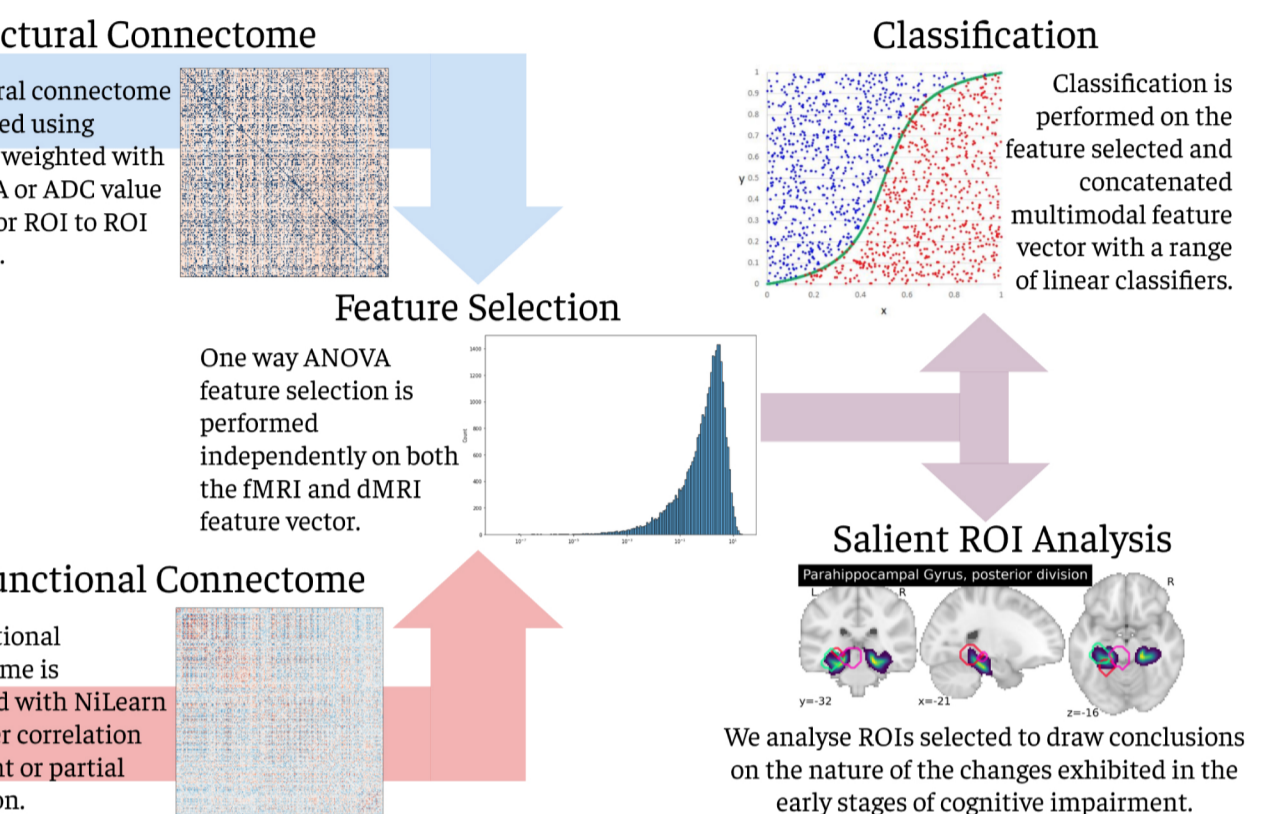


Figure 2: Summary of peak individual and multimodal performances across hyperparameters. Categories on the y-axis are grouped by hyperparameter.

## ROI Analysis

We ranked selected ROIs via a cumulative F-test across 3x10 folds for both fMRI and dMRI independently. Our fMRI analysis showed the Angular Gyrus & Middle Temporal Gyrus (temporooccipital part) to be frequently selected. Our dMRI feature selection analysis the Parahippocampal Gyrus (posterior division) & Temporal Pole. Both of these findings align with previous literature. [4], [5]

Figure 3 shows our analysis of differences in functional connectivity. We found increases in functional connectivity in all but one of the top 10 selected regions. It has been theorised that observed increases in functional connectivity within pathological populations can be explained as the brain recruiting alternative region connections in order to retain normal cognitive function. Figure 4 shows our analysis of differences in structural connectivity, demonstrating that the parahippocampal gyrus has high centrality within a dense network of altered connections from the mean CN to MCI population.