

Multimodal Fusion of MRI and SNPs for Alzheimer’s Classification

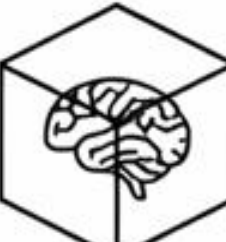
P1-001

Varsha Achuthan¹, Vishruth V Srivatsa², Thomas Gregor Issac ¹, Shweta Ramdas¹, Neelam Sinha¹

¹Centre For Brain Research, Indian Institute Of Science, India

² National Institute of Technology Karnataka ,India

A multimodal deep learning framework integrating 3D MRI volumes with SNP-based genetic signals achieved nearly 93% accuracy in Alzheimer’s disease classification, consistently outperforming unimodal baselines. Beyond diagnostic gains, the model revealed biologically relevant pathways: ANXA5 and MTR linked to apoptosis and one-carbon metabolism, SDK1 and MTMR14 associated with synaptic adhesion and autophagy, and a chromosome 19 cluster near APOE implicating epigenetic regulation and neurovascular signaling. This dual achievement demonstrates that combining imaging and genetics not only strengthens predictive power but also accelerates biomarker discovery, offering interpretable insights into the molecular and structural underpinnings of neurodegeneration.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES																				
Alzheimer’s disease (AD) is a progressive neurological disorder that leads to memory loss, cognitive decline, and structural brain degeneration. While MRI captures visible anatomical changes, single nucleotide polymorphisms (SNPs) reveal hidden genetic risks. Studied separately, these modalities provide only a partial view of disease mechanisms. Advances in multimodal deep learning now allow imaging and genetics to be fused, enabling the modeling of spatial–genetic interactions in a unified framework. Our study leverages this integration to improve Alzheimer’s classification and uncover biologically interpretable pathways, bridging structural decline with molecular regulation.	From the ADNI-1 cohort of 757 participants, 308 (137 AD, 171 CN) remained after quality control. Genetic data were normalized, imputed, and filtered to 339,255 SNPs, with 4,478 variants selected via GWAS and one-hot encoded. MRI scans underwent bias correction, skull stripping, normalization, and resizing to 152×184×152 voxels. Imaging—Genomics Pipeline  Preprocessed sMRI 3D volume Preprocessed and one-hot encoded SNP data SNP rs19345 Sub_010001 Sub_021000 Sub_030010 Sub_040100 Multimodal Classifier Top 30 SNPs Based on Brain Tissue-Specific Expression (BRAINEAC & GTEx) SNPs on Chromosome 19 (13) Pool of relevant SNPs (43 = 30 + 13) Final prioritized set for downstream analysis A multimodal deep learning pipeline integrated both modalities: SNP features were extracted using a Transformer encoder, MRI features via PeleeNet, and outputs fused through a Transformer-based Cross-Fusion Module.	The fusion model reached 93% accuracy, outperforming SNP-only (87%) and MRI-only (92%). Integrating imaging and genomics boosted diagnostic precision beyond either modality alone. <table><caption>Table 1: 5-fold Cross-Validation Performance Comparison</caption><tr><th>Average Metric</th><th>SNP-only</th><th>MRI-only</th><th>Fusion</th></tr><tr><td>Accuracy</td><td>0.8736</td><td>0.9189</td><td>0.9317</td></tr><tr><td>Sensitivity</td><td>0.8768</td><td>0.9074</td><td>0.9359</td></tr><tr><td>Specificity</td><td>0.8688</td><td>0.9013</td><td>0.9361</td></tr><tr><td>F1 Score</td><td>0.8626</td><td>0.9075</td><td>0.9217</td></tr></table> Beyond classification, the pipeline uncovered biologically meaningful signals. eQTL analysis identified genes such as ANXA5 (apoptosis regulation), MTR (one-carbon metabolism), SDK1 (synaptic adhesion), and MTMR14 (autophagy), alongside a chromosome 19 cluster near APOE, a well-established Alzheimer’s risk locus. Integrated Gradients highlighted 43 high-priority SNPs linked to apoptosis, synaptic adhesion, vascular signalling, and chromatin remodelling, bridging computational explainability with biological validation.	Average Metric	SNP-only	MRI-only	Fusion	Accuracy	0.8736	0.9189	0.9317	Sensitivity	0.8768	0.9074	0.9359	Specificity	0.8688	0.9013	0.9361	F1 Score	0.8626	0.9075	0.9217	The fusion model achieved nearly 93% accuracy across metrics, surpassing SNP-only (87%) and MRI-only (92%) approaches. This confirms that multimodal integration provides complementary information, boosting diagnostic precision beyond either modality alone. Importantly, this multimodal framework serves as a stepping stone toward biomarker discovery, offering a biologically grounded approach for identifying region-specific genetic and structural signatures of neurodegeneration. By linking computational explainability with eQTL validation, the pipeline highlights genes and pathways central to Alzheimer’s disease, reinforcing the value of combining imaging and genomics for both diagnosis and mechanistic insight.	- Alzheimer’s Disease Neuroimaging Initiative: ADNI data repository. Online Resource (2025), http://adni.loni.usc.edu, accessed: 2025-09-18 - Li, Y., Niu, D., Qi, K., Liang, D., Long, X.: An imaging and genetic-based deep learning network for Alzheimer’s disease diagnosis. Frontiers in Aging Neuroscience 17 (2025). https://doi.org/10.3389/fnagi.2025.1532470
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CONTACT				 Varsha Achuthan varshaachuthan2@gmail.com Neelam Sinha neelam@cbr-iisc.ac.in  ALZHEIMER’S ASSOCIATION AAIC>26																				