



Explainable Deep Learning In Imaging Genetics To Derive Brain-genotype Scores Associated With Cognition

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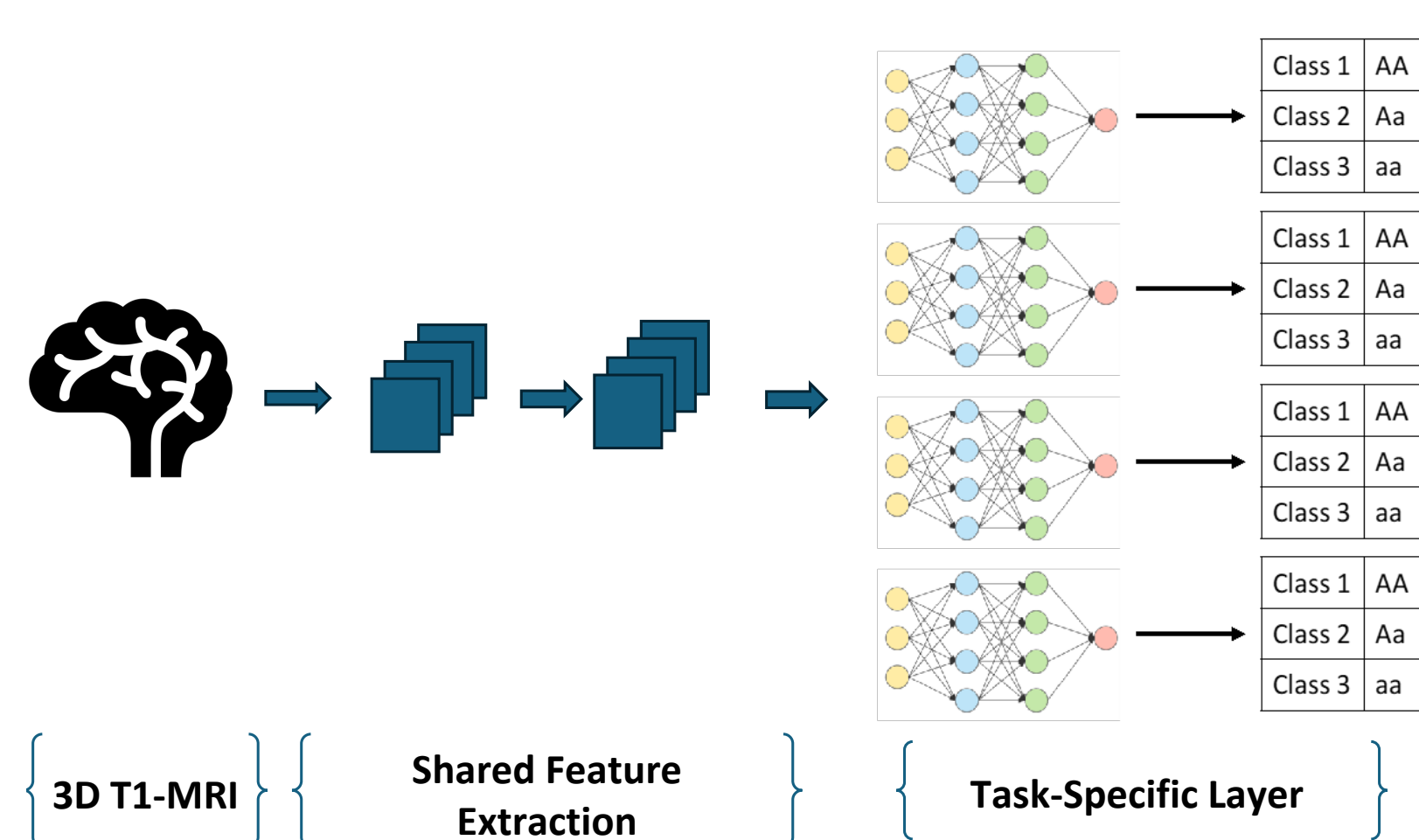


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Introduction

Imaging genetics aims to reveal how genetic variation influences brain structure and cognition. Conventional approaches often rely on predefined imaging-derived phenotypes, which compress complex MRI data into summary measures and may miss distributed or non-linear genotype-related patterns. This study introduces brain-genotype scores: MRI-derived, SNP-specific representations learned directly from structural brain images using an explainable multi-task deep learning framework. The aim is to capture biologically meaningful genotype-brain relationships and test whether these scores provide stronger links to cognitive performance than genotype data or conventional IDP-based models.

Multi-task CNN model flowchart



Dataset

Table 1. CNN Model Full Dataset split summary.

Total $N = 41\,382$		
Subset	Count	Proportion
Training	33 106	80%
Validation	4 138	10%
Testing	4 138	10%

Methods

Dataset: 40,000 UK Biobank participants with T1-weighted 3D brain MRI and genetic data. SNP selection: 120 SNPs previously associated with brain imaging phenotypes (IDPs). CNN Model: A multitask 3D CNN (modified ResNet10) classified genotype (0/1/2) for 10 SNPs per run. Brain-genotype scores were then tested as biomarkers of cognition using multiple linear regression. Comparative Models: SVM, LGBM, and logistic regression used T1 IDPs to generate brain-genotype scores and assess cognitive associations. Cognitive Analysis: Cognitive phenotypes were regressed on brain-genotype scores, adjusting for age, sex, education, and genetic PCA; F-tests assessed significance. Model Explainability: SmoothGrad saliency maps identified brain regions important for CNN genotype prediction.

CNN Model Explainability

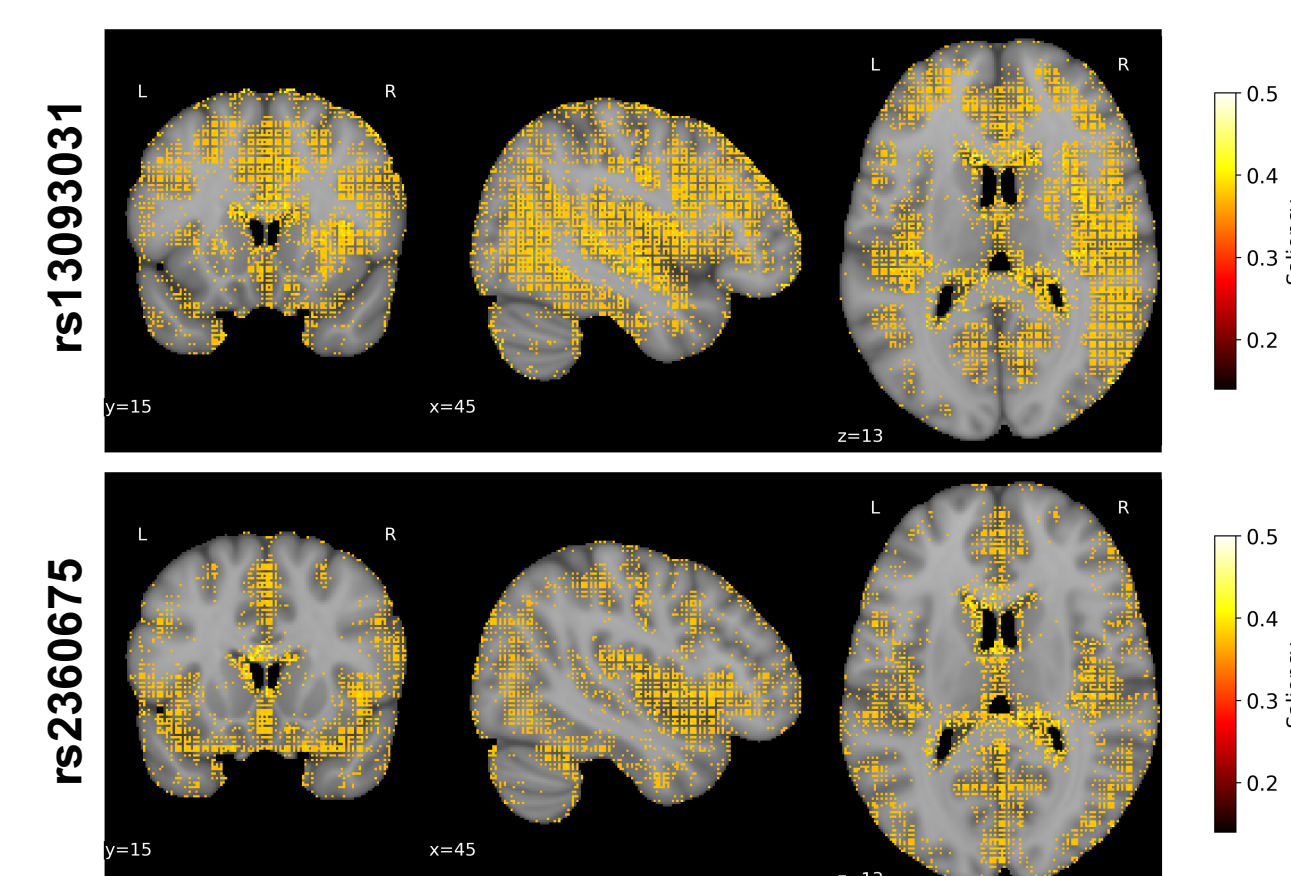


Figure 1. Average saliency maps of two representative Brain-genotype scores

Results

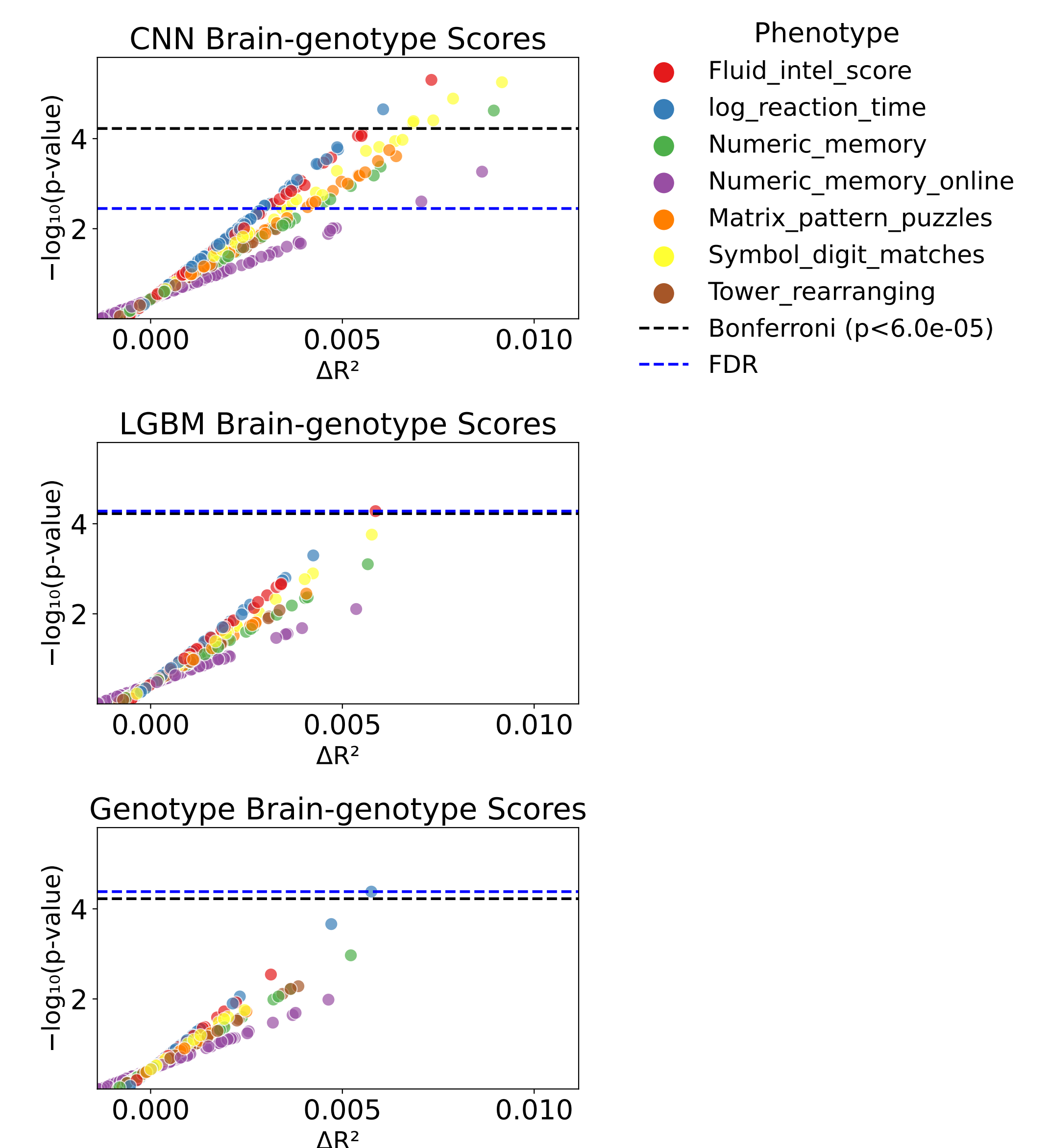


Figure 3. Effect size (ΔR^2) vs $-\log_{10} p$ scatter plot for associations between Models-derived brain-genotype scores and cognitive phenotypes.

Conclusion

We developed an explainable multitask CNN that derives brain-genotype scores from structural MRI. These scores produced 147 significant brain-genotype-cognition associations and outperformed genotype-only and classical ML models. Saliency maps highlighted biologically relevant cortical and subcortical regions, supporting the learned representations. Overall, this framework links genes, brain structure, and cognition through deep representation learning.

