Increasing the sensitivity of brain age modelling with explainable artificial intelligence

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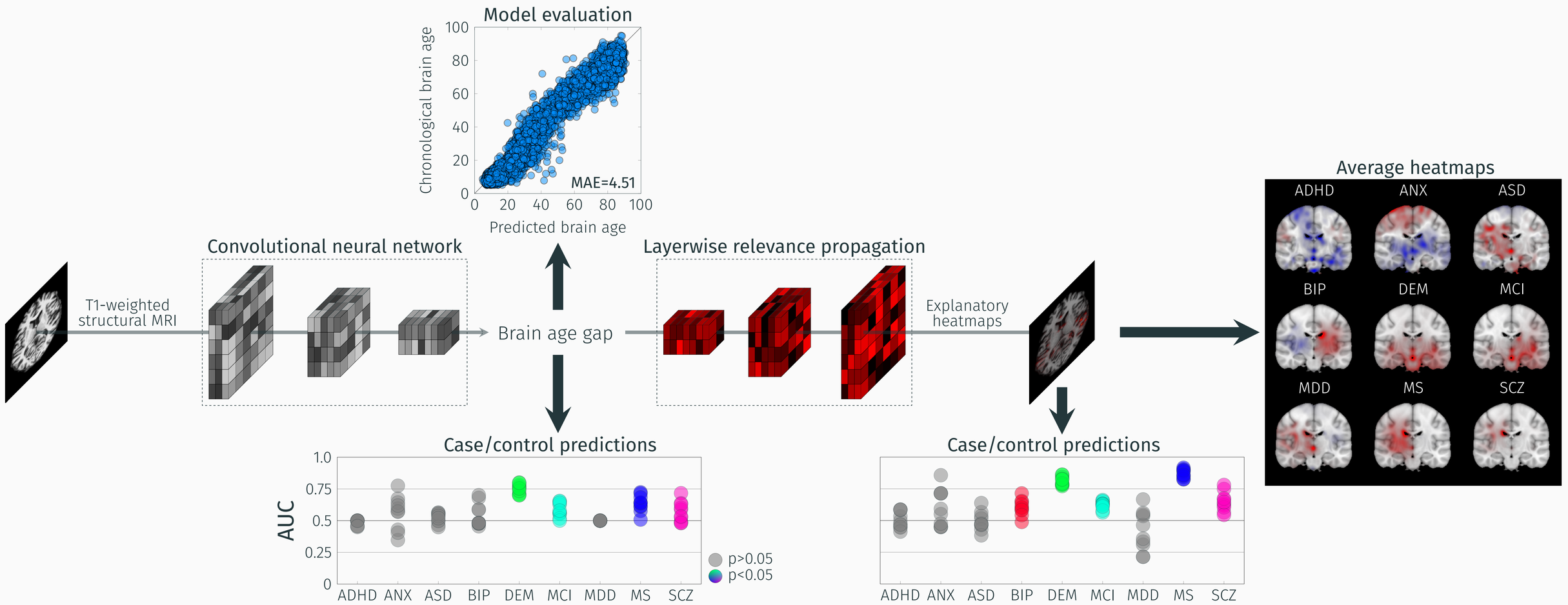

Introduction

The brain age gap (BAG), a neuroimaging-derived measure encoding the difference between the apparent and chronological age of the brain, has gained popularity as a biomarker of generalized brain health. A multitude of studies have revealed older-appearing brains in patients with various conditions[1]. However, while a discrepancy can be evident at the group-level, the abstract and summarizing nature of BAG limits its utility for precise, individualized clinical decision-making. Explainable artificial intelligence (XAI) can unveil brain regions causing deviations in BAG in the individual patient, providing a data modality that is plausibly more useful than the singular measure[2].

Methods

We trained a convolutional neural network to predict BAG using 80,007 structural magnetic resonance images from 67,881 participants. On top of the model we implemented layer-wise relevance propagation to procure heatmaps highlighting regions underlying a deviating BAG in individual participants. Finally, we investigated whether these heatmaps could support clinical decision-making across nine conditions: Attention-deficit/hyperactivity disorder (ADHD), anxiety disorders (ANX), autism spectrum disorder (ASD), bipolar disorder (BIP), dementia (DEM), mild cognitive impairment (MCI), major depressive disorder (MDD), multiple sclerosis (MS) and schizophrenia (SCZ).

Results

Our model achieved satisfactory predictive performance in a held-out dataset (mean absolute error=4.51) from unknown scanners. Singular BAGs from our model allowed us to meaningfully discriminate patients from controls (mean area under the receiver operating curve (AUC)>0.5 in a nested 10-fold cross-validation, $p<0.05$) for four out of nine diagnoses (DEM, MCI, MS, SCZ). The heatmaps yielded significantly improved predictions (mean AUC_{map}>mean AUC_{BAG}, $p<0.05$) for five out of nine diagnoses (BIP, DEM, MCI, MS, SCZ). Visual inspection of average heatmaps per patient cohort revealed that the highlighted regions varied notably between conditions.

Conclusion

Enhancing brain age models with XAI techniques introduces a new, derived, data modality that is more sensitive towards subtle aberrations in neuroimaging data than a singular brain age prediction.

References

1. Franke, K. & Gaser, C. Ten Years of BrainAGE as a Neuroimaging Biomarker of Brain Aging: What Insights Have We Gained? *Frontiers in Neurology*, 2019
2. Martin S.A. et al. Interpretable machine learning for dementia: A systematic review. *Alzheimer's Dementia*, 2023